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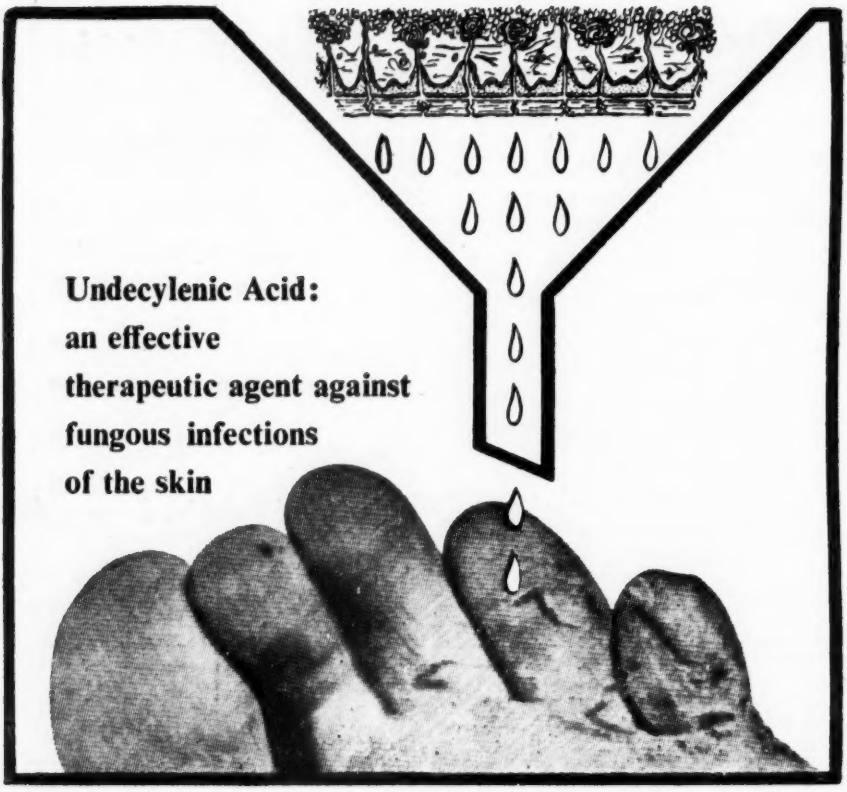

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Granuloma Venereum and its Relationship to Epidermoid Carcinoma

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Granuloma Venereum is a chronic slowly progressive and mildly contagious disease with a predilection for the stratified epithelium of the external genitals and its neighbourhood, and less frequently of the labial and bucco-pharyngeal regions of the body. The disease is characterised by the development of exuberant granulation tissue in the corium with subsequent ulceration and with little or no tendency to spontaneous healing. It is a misnomer to call it Granuloma Inguinale, as the primary seat of affection is in the external genitalia in over 90% of observed cases. It is generally considered as a venereal disease and almost exclusively occurs in people of low socio-economic status of promiscuous sexual habits and poor personal hygiene. We prefer to call the disease 'Granuloma Venereum'. The condition should be distinguished from the other venereal disease, Lymphogranuloma Venereum, which is caused by a virus and is an affection of the lymph nodes and lymphatics of the external genitalia and ano-rectum.

The causative agent of the disease is the Donovan body first described by Donovan in 1905 (Fig. 1). Compounds of antimony were the standby in the treatment of the disease during the past 35 years. But the long term results of antimony therapy were disappointing. Relapse, progression and treatment resistance were frequent. Since 1947, the newer anti-biotics, Streptomycin, Aureomycin, Chloramphenicol, and Terramycin have proved to be of great therapeutic value, both individually and/or in combination.

The relationship of Granuloma Venereum to Epidermoid Carcinoma has of late been exercising the minds of students of the subject. A few contributions and case reports have appeared in the American literature[2-12]. Beerman and Sonck,[13] in a paper read before the Tenth International Congress of Dermatology,

subsequently published in the American Journal of Syphilis, Gonorrhoea and Venereal Diseases, have focussed attention on the subject and stimulated the authors of this paper to review the case records of nearly 2000 cases of Granuloma Venereum treated at the Venereal Diseases Department of the Government General Hospital, Madras, over a twenty year period. Following the lead of Beerman and Sonck,[13] three questions may be posed for discussion:

1. Does Granuloma Venereum simulate Cancer?
2. Does cancer develop as a complication on a preexisting Granuloma Venereum?
3. Do cancer and Granuloma Venereum occur independently in the same patient at the same site?

A study of the literature and our experience suggest that the resemblance between the two lesions may be close both on clinical and histological grounds. Granuloma Venereum has been mistaken for cancer more frequently than cancer for Granuloma Venereum. The threshold of suspicion for Granuloma Venereum on the part of the average surgeon and gynaecologist is rather low, even in endemic areas; and it is not uncommon for mutilating operations being performed on patients in the mistaken diagnosis of the lesion for cancer. Figures (2) and (3) represent granulomatous lesions on the anterior aspect of the scrotum in place of the penis and extensive fleshy nodular lesions round the opening of the implanted urethra in the perineum of a patient who sustained an amputation of his penis for a supposed cancer. Tissue smears from both the lesions showed typical intracellular Donovan organisms and the lesions healed with Streptomycin. Kern's[14] report of three cases where squamous-cell carcinoma simulated Granuloma Venereum even in the presence of Donovan organisms in two of the cases, is an example of the reverse mistake in diagnosis. The clinical appearance of a chronic long-standing Granuloma Venereum may closely mimic that of an epidermoid carcinoma in the exuberant fleshy growth or in an ulcer with nodular base and everted edge.

In common with other chronic granulomas of the integumentary system such as syphilis, tuberculosis, yaws, mycotic infection etc., a pseudo-epitheliomatous hyperplasia of the marginal epithelium is a characteristic histological feature of Granuloma Venereum. Figures (4), (5), (6), (7) and (8) are microphotographs of various grades of pseudo-epitheliomatous hyperplasia in Granuloma Venereum, Yaws and Syphilis.

Beerman and Sonck[13] have reported epithelial changes in 97 cases of Granuloma Venereum. With the exception of 2 specimens all the other 95 sections examined by them showed a moderate to marked acanthosis with pseudo-epitheliomatous changes. But it is useful to remember that the specific diagnostic histological feature of the disease is in the corium showing a massive cellular

reaction consisting of plasma cells, polymorphonuclear leucocytes, eosinophile leucocytes and scattered large mononuclear cells with or without the Donovan organisms (Fig. 9). The predominance of polymorphonuclear leucocytes in the superficial part of the ulceration along with the invasion of the prickle cell layer by the same leucocytes is another feature of Granuloma Venereum, which is not usually the case in squamous-cell epithelioma.

In some cases of Granuloma Venereum of long-standing, there may be an extreme hyperplasia and proliferation of the epidermis in an irregular manner with narrow strands of prickle cells, reaching deep into the cutis, with even pearl formation, histologically resembling Grade I squamous-cell epithelioma and the final diagnosis depends on the clinical outcome to antibiotic therapy. With a multiplicity of effective therapeutic agents, such as Streptomycin, Aureomycin, etc., failure to achieve cure must cast serious doubt on the validity of diagnosis of Granuloma Venereum.

On the second and third questions whether epidermoid carcinoma occurs as a complication of or sequel to Granuloma Venereum and whether the two conditions may occur independently in the same patient, opinions are not unanimous.

The incidence of epithelioma arising from other conditions which include syphilitic, tuberculous and varicose ulcers, ano-rectal lymphogranuloma, scar of burns and certain pre-cancerous dermatoses, varies from a fraction of 1% to a maximum of 6% according to Ormsby and Montgomery[15]. It is likewise conceivable that carcinoma may supervene on a lesion of longstanding Granuloma Venereum for the same reason that it occurs in other chronic cutaneous granulomatous conditions. It is also pertinent to point out that both Granuloma Venereum and epithelioma of the external genitalia, particularly of the penis, occur more frequently in that section of the population with a low socio-economic status and poor personal hygiene. In the United States according to Lenowitz and Graham[16] quoted by Bleich,[17] carcinoma of penis is five times as common among Negroes as among white persons. Similarly the incidence of Granuloma Venereum is about 88% among Negroes and 12% among the poorwhites of America as reported by Clarke[18]. In South India the incidence of carcinoma of penis constitutes about 16% of total cancers occurring in men and is probably the highest in whole of the Indian Republic[19]. Likewise South India is the endemic reservoir for Granuloma Venereum.

The study of the titles of the case reports that have appeared in the American literature such as "Granuloma Inguinale simulating Carcinoma",[2] "Granuloma Inguinale ? Carcinoma",[9] "Granuloma Inguinale clinically diagnosed as Carcinoma",[8] "Carcinoma simulating Granuloma Inguinale",[14] reveals the difficulty, doubt and the mistakes that have occurred in the differential diagnosis of the two conditions. Chen, Greenblatt and Dienst,[20] in a study of 95 cases of Granuloma Venereum reported 6.3% showed cancer histologically.

Clearkin[21] in his study of Granuloma Venereum at Trinidad makes a general observation that " Epidermoid carcinoma in the ano-genital region in comparatively young subjects is not uncommon in Trinidad and is often associated with with Granuloma Inguinale. " In several of his cases, biopsy from one portion of the lesion revealed carcinoma, and from another, granuloma inguinale.

' Post Hoc-Propter Hoc.' reasoning has been rather uncritically applied in many of the reported cases. Combes[11] and more recently Mackap and Bunch[12] have reported cancer developing on an old granuloma inguinale which in our opinion seems to satisfy the rigid criteria of correct diagnosis of an earlier granuloma, a response to treatment and subsequent development of cancer verified clinically and histologically. We consider that a true epitheliomatous change may occur as a late complication of or a sequal to long-standing Granuloma Venereum, but this seems an infrequent occurrence.

The association of cancer and Granuloma Venereum occurring in the same patient has been recognised by us as affecting the penis in the male and cervix in the female. The occurrence in our opinion seems to be merely sequential without any implication of causality. In some of the reported cases and also in two patients in our study to be described below, it would seem that cancer was the earlier lesion chronologically and that Granuloma Venereum was a later superimposed infection. The demonstration of Donovan organisms in such cases and the apparent partial involution of the lesion after specific therapy do not prove anything. These patients come back with unhealed progressive lesions to further antibiotic therapy, with involvement of the regional lymph nodes and the histological features of an infiltrating squamous-cell epithelioma. Beerman's[18] recent case report of a 41 year male Negro who was treated for a painful lesion on the ventral aspect of the prepuce is a perfect example where, inspite of the initial histological diagnosis of a Grade I squamous cell epithelioma and the absence of Donovan organisms from the lesion, the patient was subjected to a multiplicity of therapeutic procedures-Sulphonamides, Penicillin, local application of Podophyllin, treatment with Streptomycin, in succession for a period of nearly 18 months without any appreciable change in the clinical progression of the disease. The diagnosis of a squamous-cell epithelioma was ultimately accepted and amputation of the organ was performed.

With this short introduction, the authors of the paper present 5 cases of epidermoid carcinoma in association with Granuloma Venereum observed by them among the 2000 cases of Granuloma Venereum who attended the Venereal Diseases Department of the Government General Hospital, Madras, during a a period of 20 years.

Case No. 1: A male aged 35 years attended the department in 1931 with a small hypertrophic type of granulomatous ulcer of six months' duration at the peno-scrotal junction. It was clinically diagnosed as Granuloma Venereum. No

attempt was made to confirm the diagnosis by the demonstration of Donovan organisms in tissue smears. He received a course of tartar-emetic injections and the ulcer was completely healed in 18 days. He disappeared from observation for a period of 12 years and reported in 1943 with a raised indurated ulcer at the site of the old healed granuloma at the peno-scrotal junction. The duration of the ulcer was stated to be nine months. Mistaking the condition for a recurrence of the old disease, he has been treated at different hospitals with antimony but without benefit. When he came under our observation in 1943 his old record was unearthed and reviewed. The smear examination for Donovan organisms was repeatedly negative though the lesion presented a superficial clinical resemblance to Granuloma Venereum. A biopsy was taken and sent for histopathological examination. The report was " squamous cell epithelioma ". The patient was referred for further treatment to the surgical side of the hospital.

Case No. 2: A male aged 52 years was referred to the Venereal Diseases Department, Government General Hospital, Madras, from one of the surgical units of the hospital on 15-7-1939 for ulceration of the external genitalia. On examination, the dorsal portion of the foreskin of penis was a mass of hyperplastic ulcerated tissue situated like a hood over the glans penis. A large granulomatous ulcer was present on the anterior surface of the skin of scrotum which was elephantoid. It is recorded in the case card of the patient that the ulceration looked like Granuloma Venereum in one area and had the clinical appearance of cancer in another area of the lesion. Tissue smears for Donovan organisms were repeatedly negative. Kahn and Wassermann tests of serum were reported strongly positive. Frei intra-cutaneous test for Lymphogranuloma Venereum was negative. The report on the biopsy sent from the surgical unit prior to the patient's coming under our observation, was " Marked hyperplasia of the stratified epithelium with sub-epidermal fibrosis and scattered collection of plasma cells and round cells in the dermis. The picture is that of a chronic granuloma ". The condition was diagnosed as Granuloma Venereum of the hyperplastic type and specific treatment with ' Fouadin ' was started. Before any improvement could be noticed, the patient stopped away from treatment. On 29-9-1942, three years after his first visit to the hospital, he reported again. This time, the ulceration had progressed involving the entire penis encircling the root and spreading over the anterior surface of the scrotum. The penis was deformed and twisted with the glans turned horizontally to the left. The lesion over the dorsal aspect of the penis and adjacent portions of the root and scrotal skin on the right side of the former presented the clinical appearance of a fungating nodular neoplastic growth, while the area of ulceration on the anterior surface of the scrotum below the penile root clinically looked like Granuloma Venereum. Two specimens for biopsy were taken, one from the advancing lower edge of the scrotal ulceration and the other from the dorsal area of the growth

on the shaft of the penis. In addition to the lesions on the genitalia, granulomatous ulceration of the left half of the palate was discovered which was not present in 1939.

Smear from the different parts of the lesions were negative to Donovan organisms; but contained plenty of fusospirillary organisms. Search for Donovan organisms was not repeated. He received a adequate course of treatment with antimony. The palatal ulceration was completely healed, but the the genital condition did not show any improvement. The patient was transferred to the care of a Surgeon who excised the whole area of disease. Figure (10) is a photograph of the excised ulcerated growth of the penis and scrotum.

Figure (11) is a microphotograph of section examined from the scrotal lesion of Case No. 2 showing marked acanthosis with thickening of the epidermis, and diffuse infiltration of the corium with round and plasma cells. The histological diagnosis is chronic granuloma.

Figur (12) is a microphotograph of section taken from the penile lesion of case No. 2 showing squamous cell epithelioma with limited keratinization and ulceration.

Case No. 3. A married woman aged 35 years was referred to the Venereal Diseases Department of the Govt. General Hospital, Madras, on 24-5-1943 from another hospital with a lesion on the vulva and with the history of having been treated at the latter institution for Granuloma Venereum.

Physical examination revealed a soft velvety granulomatous ulcer about 1.5 centimeters in diameter in the upper part of the right labium majus adjacent to the root of the clitoris. Kahn and Wassermann reactions were positive though there was no clinical evidence of history of syphilis. The regional lymph nodes were not palpable. A tissue smear from the ulcer was positive to Donovan organisms. In view of the unsatisfactory response of the lesion to tartar emetic injections, a year and a half ago, a combined therapy was instituted consisting of 'Fantorin' intramuscularly and superficial X-rays to the ulcer. The 'Fantorin' had to be discontinued after about eight injections as the patient showed signs of intolerance to the drug; but superficial X-ray therapy was continued to a total of fifteen exposures. There was partial involution of the lesion. The patient was discharged with instruction to report after a month. On 26-10-43 she reported at the clinic for a check up. A residual flat ulcer of slightly reduced size was still observed at the upper end of the right labium majus. Smears for Donovan organisms were negative this time. She received a prolonged course of treatment with another antimonial compound, 'Anthiomaline' for a little over two months. The ulcer was completely healed. On 11-1-1944 she was discharged from the hospital and advised to report if there be any recurrence of the trouble. She did not report at the department, but it was ascertained that she

was admitted in another hospital in March 1947 for recurrence of the ulcer at the same site and that a biopsy from the ulcer was reported as 'carcinoma of sebaceous glands'. The further history of the patient was not clear except that she died ultimately of anaemia and cachexia.

Case No 4. A male aged 72 years was referred to the Venereal Diseases Department of the Government General Hospital, Madras, from the Cancer Clinic on 23-6-1950 for opinion on a penile lesion. On eliciting the history, the patient stated that he had been noticing a nodular painless thickening of the foreskin for about four years and only three months ago he developed the present painful ulceration; he had been living in sexual relationship with a mistress for ten years and had noticed a similar lesion in her genitalia. Physical examination revealed a fleshy easily bleeding granulomatous ulceration all round the edge of the foreskin which was not retractable. The regional lymph nodes were slightly palpable, somewhat hard but discrete and painless. Extensive hypo-pigmented anaesthetic patches were found all over the face, trunk, and limbs with a perforating ulcer on the sole of the right foot. A specimen for biopsy was taken at the Cancer Clinic from the preputial ulceration for histopathological examination before the patient was sent to the Venereal Diseases Department. A tissue smear from the lesion showed typical intra-cellular Donovan bodies, both young and growing forms. The laboratory investigations for other venereal diseases were negative but smears from skin clips of an anaesthetic patch were positive to lepra bacilli. The Kahn and Wassermann reactions of the blood were negative. The report of the biopsy specimen sent from the Cancer Clinic was 'chronic granuloma with epithelial hyperplasia'. On the basis of the clinical and histological findings, the condition was diagnosed as Granuloma Venereum. The patient was given 20 Gms. of Streptomycin intramuscularly for a period of eighteen days. The preputial ulceration was healing rapidly and to relieve the phimotic condition of the prepuce a circumcision was performed on the last day of therapy (1-8-50) and the specimen was sent for routine histopathological examination. The post operative wound was reported healing on 5-8-50 and the patient was discharged from hospital and advised to attend the clinic as an out-patient. He failed to report for three weeks and on 28-8-50 presented himself with a raised nodular unhealed post operative ulceration on the ventral aspect of the glans penis, which clinically looked like epithelioma. Smears for Donovan organisms were negative this time. The second biopsy report on the circumcised prepuce was, "The epithelium apart from being hyperplastic with irregular down-growth, shows features of intra-epithelial malignancy. In some parts of the section detached sheets of epithelial cells have grown deep into the dermis and show mitosis and giant nuclear forms. At this stage the condition should be regarded as squamous cell carcinoma."

Figure (13) is the microphotograph of the section from the first biopsy with slight hyperkeratosis with elongation of retepegs. Corium diffusely infiltrated with round and plasma cells. The histological diagnosis is chronic granuloma.

Figure (14) is the microphotograph of the section of the second biopsy from the same patient. Diagnosis–squamous cell carcinoma–vide supra for the the detailed report of the Pathologist. The patient was referred to the Cancer Clinic on 2–10–50 and was advised to undergo deep X–ray therapy. He evidently failed to follow the advice. When he came again to the Venereal Diseases Department on 29–1–51 in response to the call of the Social Worker, the lesion had progressed fairly rapidly involving the entire glans penis and part of the shaft. He failed to turn up again and it was reported that he died a few months afterwards.

Case No. 5. A male aged 30 years was first seen at the Venereal Diseases Department on 2–2–52 with genital ulcers of two years' duration. Denied having had any extra marital sexual contact during the previous six years.

Physical examination revealed the following lesion: (a) The prepuce was swollen, hard and globular with granulomatous ulceration at the edge and a fistulous indurated opening at the posterointerior surface, discharging thick chocolate coloured fluid. (b) A bat wing shaped crusted ulceration extending from the pubic region on to either side of the groin. (c) A raised granulomatous ulceration on the anterior part of the upper gum region with oedema of the upper lip. The Kahn and Wassermann reactions of the blood were negative. Smears from the penile, groin, and mouth lesions were at first negative to Donovan organisms and showed plenty of fusospirillary and other banal organisms. Preliminary treatment with penicillin cleared the ulcers of the secondary contaminants and smears taken on the fourth day from all the three lesions revealed typical intra–cellular Donovan organisms with many of the mononuclear cells heavily parasitised. A biopsy was not taken at this time. 20 Gms. of Streptomycin were given for ten days at the rate of 1 Gm. I. M., twice a day. The patient was discharged on 11–3–52 with the lesions completely healed. He was advised to report a few weeks later for a check up and to undergo a circumcision for the phimotic condition but he reported only on 28–8–52 in a bad state. The entire prepuce had been destroyed and in its place was seen an irregular nodular ulceration involving the coronal sulcus and the adjoining part of the glans with everted edges. The skin of the shaft of the penis and that of the scrotum were elephantoid. But the groin and mouth lesions were completely healed without any evidence of breaking down. Smears from the penile lesion were repeated negative to Donovan organisms. At this stage the clinical appearance was that of a rapidly progressing epithelioma. A biopsy was taken and was reported as 'Keratinising squamous cell epithelioma.'

Figure (15) is a clinical photograph of the cancerous penile lesion with healed granuloma of the groins. Figure (16) is a microphotograph of the section showing a typical keratinising squamous cell epithelioma.

COMMENT

In cases No. 1 and 3 it would appear that epidermoid carcinoma occured as a sequel to a pre-existing granuloma at the same site. The initial diagnosis of Granuloma Venereum in either case was presumed to be correct on clinical grounds and the complete healing of the lesions in both patients with specific therapy. A remarkable feature of Case No. 1 is that nearly 12 years elapsed before the development of epithelioma from the scar of the healed granuloma at the peno-scrotal junction. In Case No. 3 it is also presumed that between 1943 and 1947 she was free of any lesion and that carcinoma developed on the scar of the old granuloma three years after the original infection was cured.

In case No. 2 an initial diagnosis of Granuloma Venereum was made on clinical and histological appearance of the lesion. The effect of an adequate specific treatment could not be observed as the patient defaulted after a few injections. When he turned up in 1942, three years after his first visit, the extensive nodular ulceration involving the penis and scrotum left no doubt as to the cancerous nature of the condition, although in some places, the ulceration simulated Granuloma Venereum. Donovan organisms were never demonstrated in the lesions either on the first or on the subsequent visits. But during the second visit, ulceration of the left half of the palate was for the first time noticed. Treatment with ' Anthiomaline ' was given the second time. The palatal ulceration rapidly healed but the genital condition was unchanged. Biopsy from one portion of the genital ulcer showed granuloma while that from another portion typical invasive epithelioma. We are led to infer that Granuloma Venereum preceded the development of cancer in the genitalia. The secondary occurrence of granuloma in the palate three years after its appearance in the genitals and the successful response to specific therapy lends support to the inference.

In case No. 4 the advanced age of the patient, a definite history of a painless thickening of the prepuce which the patient had noticed for four years, the unhealed post-operative wound, the histological report of squamous cell epithelioma on the circumcised foreskin are indicative of an earlier unrecognised epithelioma. The ulceration of the preputial edge, the first biopsy report, the finding of Donovan organisms from the ulcer and the apparent healing of the ulcer after Streptomycin therapy are compatible with the diagnosis of Granuloma Venereum. But the latter infection was only of three months' duration and seems to us to be a subsequent superimposed infection on the foreskin which had already undergone a neoplastic change. Certain precancerous conditions such as Erythroplasia of Queyrat and leukoplakia occur in the mucous membrane of the prepuce and the glans with or without phimosis. Clinically many of these lesions persist for years

without any signs of malignant change, although histologically they may display the features of squamous cell epithelioma *in situ*. It is conceivable that the occurrence of Granuloma Venereum with its tendency to induce marked epithelial hyperplasia on the site of erythroplasia of prepuce or glans may convert a comparatively benign stationary epithelioma *in situ* into an infiltrating invasive type of squamous cell epithelioma.

In recent studies of scars of healed Granuloma Venereum of the genitalia, we have been noticing a persistent thickening of the area with a tendency to leukoplakic changes in some cases. Histopathological studies are under progress and will form the subject of another paper.

In case No. 5 the three separate lesions of the penis, groin and gums were diagnosed as Granuloma Venereum on the basis of the clinical appearance and finding of Donovan organisms in smears and the rapid therapeutic response to streptomycin therapy. Five months after he was discharged 'healed', the patient reported with a clinically typical nodular ulceration which had destroyed the prepuce and spread to the corona and adjoining areas. But the scars of the healed lesions of the groin and gums showed no evidence of breaking down. In this patient as in case No. 4, it is our impression that a malignant change might have occurred in the penis, before he developed a superimposed infection with granuloma venereum.

The incidence of squamous cell epithelioma occurring either as a complication of, sequel to, or in association with Granuloma Venereum is one-fourth of 1% among 2000 patients diagnosed and treated at the Venereal Diseases Deparment. It has been our experience that it is risky to depend merely on the histological diagnosis of squamous cell epithelioma when biopsy specimens from the external genitalia are sent for histopathological examination. Marked and irregular epithelial hyperplasia, simulating neoplasia histologically, in the genital lesion of a young person should alert the clinician that the condition may be Granuloma Venereum. The mistaken diagnosis of cancer in the penis based on histology alone in this part of the country where Granuloma Venereum is endemic has cost many a patient a cruel unjustifiable ablation of the most important member of his anatomy. We have records in many instances where such tragedies have happened. To prevent the recurrence of such errors the closest collaboration between the Clinician and the Pathologist is essential.

SUMMARY

A discussion based on a review of the available literature on the relationship of Granuloma Venereum to cancer is presented. Five cases of squamcus cell epithelioma occurring either as a complication or in association with Granuloma Venereum are reported.

(Continued on Page 19)

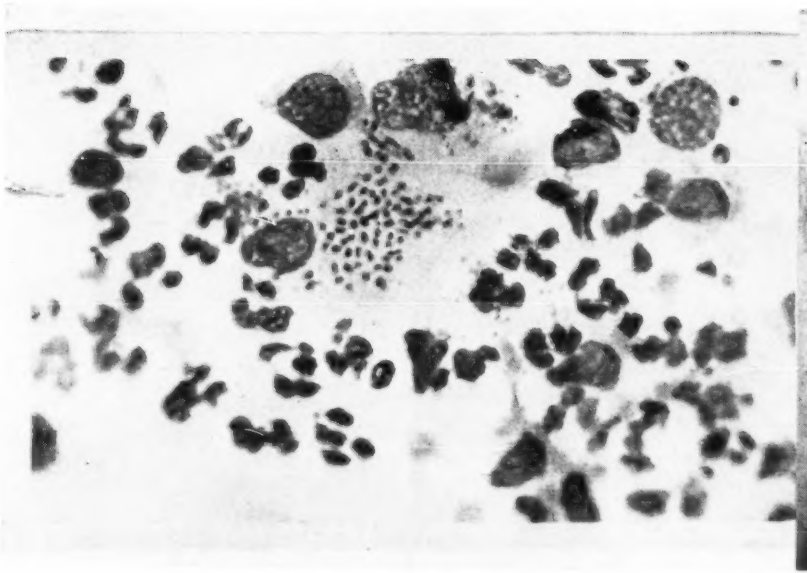

Fig. 1

Fig. 2.

Fig. 1 High power microphotograph of stained tissue smear from a lesion of Granuloma Venereum showing a cluster of encapsulated Donovan organisms in the cytoplasm of a mononuclear cell.

Fig. 2 Photograph of Granuloma Venereum on the front of the scrotum at the site where the penis ought to have been and extension of the lesions to the groins and cruro-scrotal fold from the perineum.

Fig. 3.

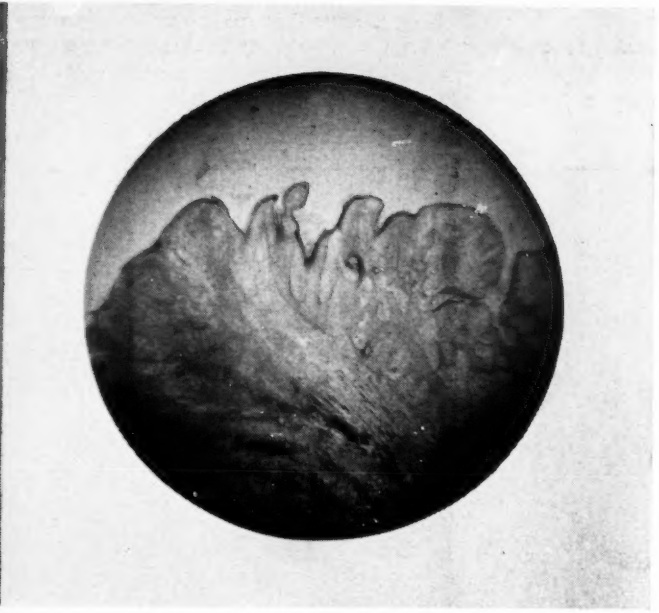

Fig. 4.

Fig. 3 Photograph of Granuloma Venereum around the opening of the artificial urethra in the perineum in the same patient as Fig. 1.

Fig. 4 Low power microphotograph of pseudo-epitheliomatous hyperplasia Grade I in a case of Granuloma Venereum. Marked acanthosis with elongated and curved retepegs invading the dermis. Basement membrane unbroken. Intra epidermal collection of leucocytes.

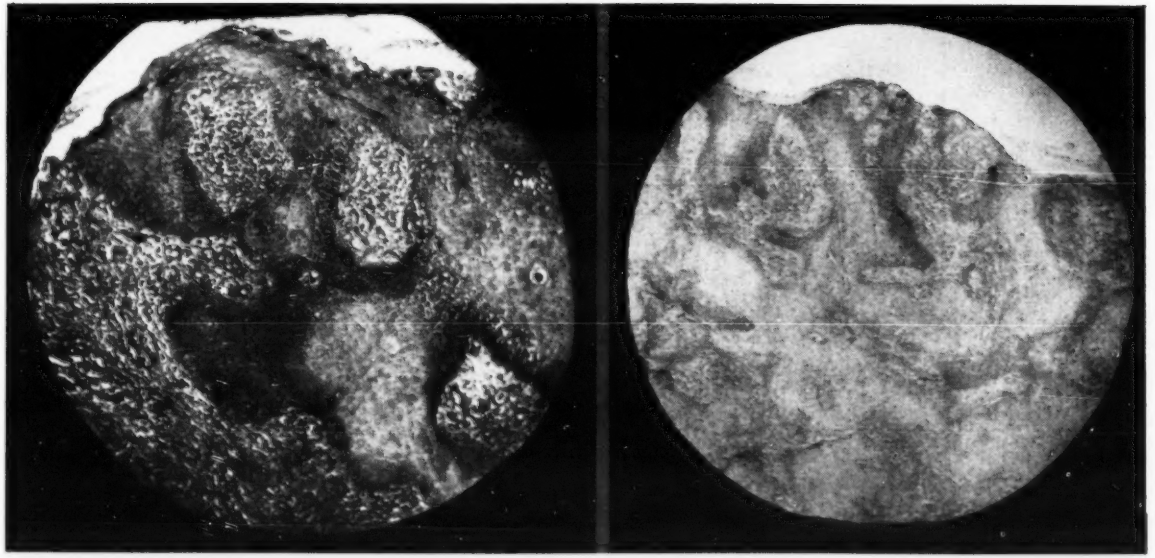

Fig. 5. Fig. 6.

Fig. 5 Low power microphotograph of pseudo-epitheliomatous hyperplasia Grade II in a case of Granuloma Venereum. Marked acanthosis with a tendency to pearl formation. In spite of the irregular epithelial downgrowths the integrity of the basal layer is maintained. Abundant sub-epidermal inflammatory cells.

Fig. 6 Low power microphotograph of pseudo-epitheliomatous hyperplasia Grade III in a case of Granuloma Venereum. Acanthosis but with markedly irregular and riotous downgrowth of epithelium with indistinct and blurred basal layer. Moderate sub-epidermal collections of inflammatory cells.

Fig, 7. Fig. 8.

Fig. 7 Low power microphotograph of pseudo-epitheliomatous hyperplasia Grade II in a case of Yaws. Acanthosis, retepegs irregularly elongated with a tendency for inter-communication forming a sort of network. Infiltration with polymorphonuclears in the lower epidermis and contiguous papillae.

Fig. 8 Low power microphotograph of pseudo-epitheliomatous hyperplasia Grade I in a case with syphilitic condyloma. Marked epithelial hyperplasia, acanthosis and papillomatosis. Basal layer distinct. Inflammatory cells are chiefly round and plasma cells.

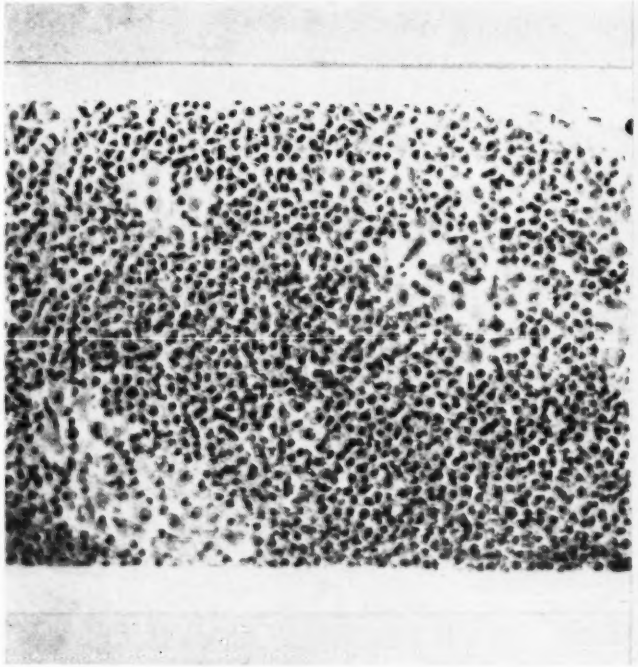

Fig. 9.

Fig. 10.

Fig. 9 High power microphotograph of the corium showing a massive cellular reaction. Note the number of mononuclear cells containing faintly staining Donovan organisms in the cytoplasm.

Fig. 10 Photograph of the excised, ulcerated growth of the penis and scrotum from Case No. 2.

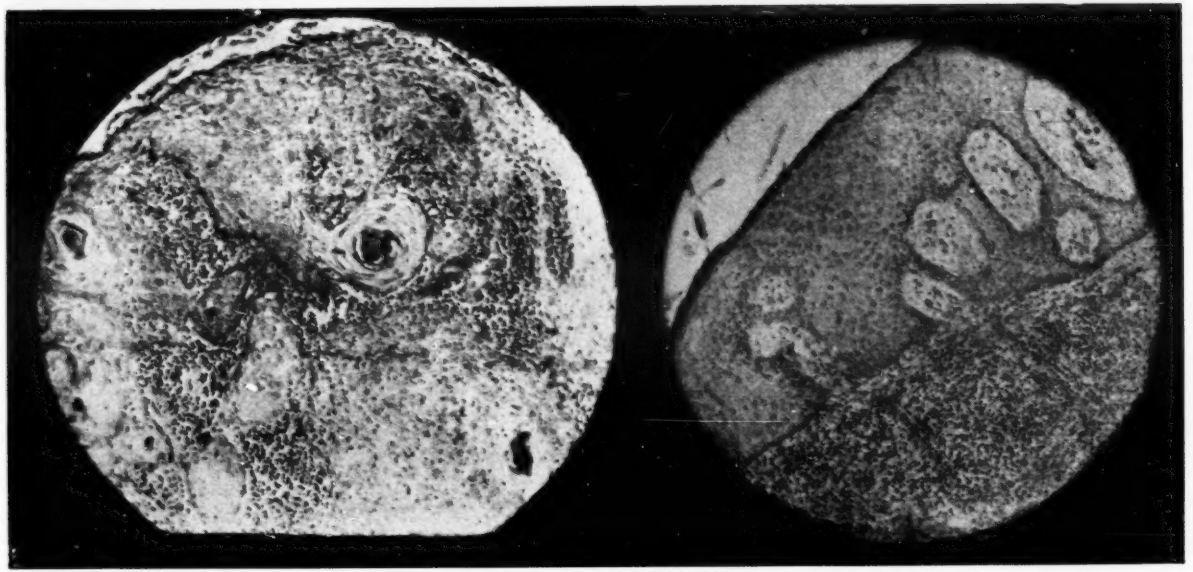

Fig. 12. Fig. 11.

Fig. 11 Low power microphotograph of section examined from the scrotal lesion of Case No. 2 showing moderate acanthosis with thickening of the epidermis. Diffuse infiltration of the corium with round and plasma cells. The histological diagnosis is chronic granuloma.

Fig. 12 Low power microphotograph of section taken from the penile lesion of case No. 2 showing squamous cell epithelioma with limited keratinization and ulceration.

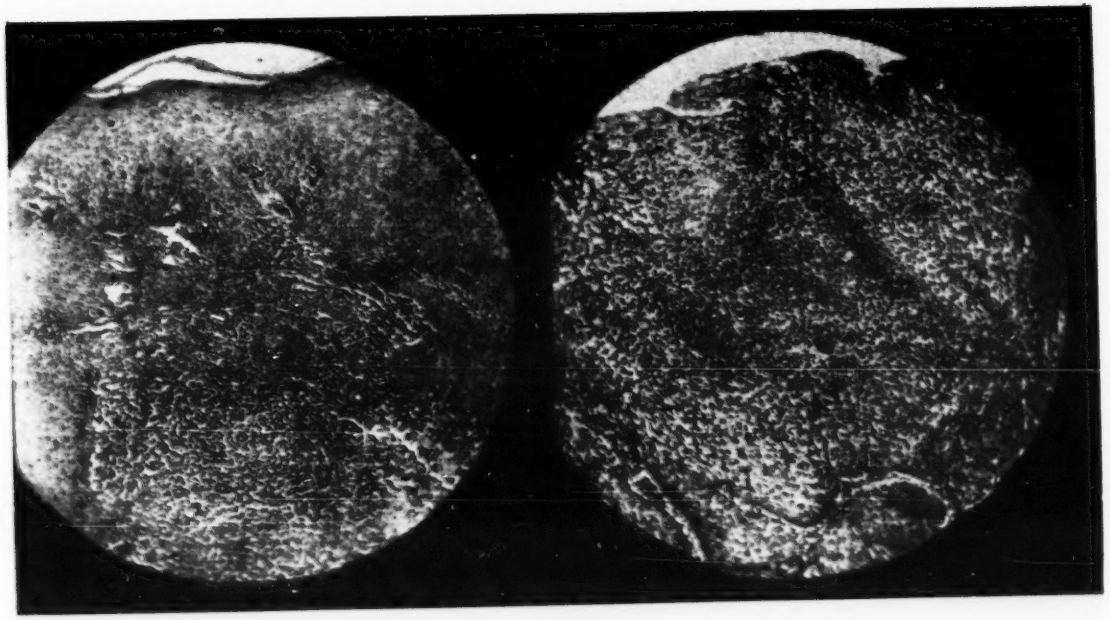

Fig. 13. Fig. 14.

Fig. 13 Low power microphotograph of section from the first biopsy in case No. 4. Slight hyperkeratosis, acanthosis with elongation of retepegs. Corium diffusely infiltrated with round and plasma cells. The histological diagnosis is chronic granuloma.

Fig. 14 Low power microphotograph of section from the second biopsy in the same patient as Fig. 13. Diagnosis: squamous cell carcinoma.

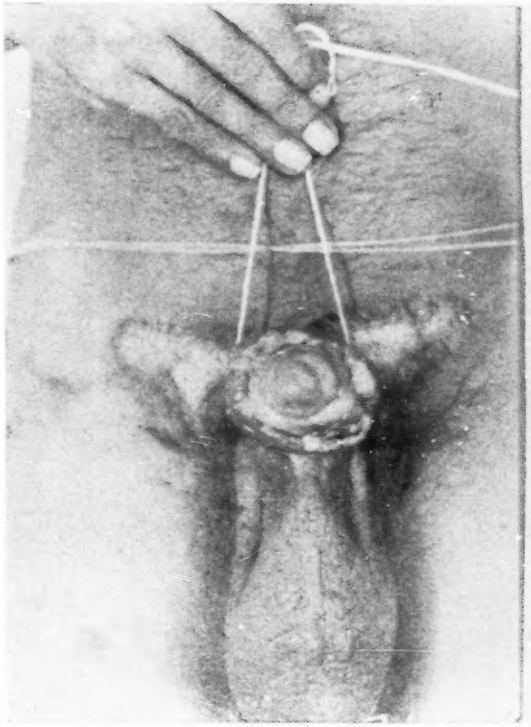

Fig. 15.

Fig. 16.

Fig. 15 A clinical photograph of the cancerous penile lesion with healed granuloma of the groins.
Fig. 16 A microphotograph of the section showing a typical keratinising squamous cell epithelioma.

The authors thank the Dean of the Government General Hospital and Madras Medical College for permission to use the records of the Medical College and the Hospital. We are indebted to Professor D. Govinda Reddi, Professor of Pathology, Madras Medical College, for the histological reports and Dr V. C. Anguli, Tutor in Pathology, for helping to take the microphotographs.

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KNOWLEDGE FROM WORLD CONTEMPORARIES

Some Practical Clinical Aspects of Leprosy

Of the great infectious diseases of mankind, that probably least known to the American physician is leprosy. Confined largely to the tropics and to areas where hygienic conditions are poor, leprosy is seldom seen by the practitioner in the continental United States. Nevertheless, a disease which affects about 5,000,000 human beings cannot be allowed to fall into the professional subconscious

PHYSICAL SIGNS

The most common physical findings on original physical examination were a fixed dermatosis, enlarged peripheral nerve trunks, and a congested nose. These phenomena follow from the fact that *Mycobacterium leprae* confines its pathogenic activities largely to the skin, peripheral nervous system, and upper respiratory tract.

From a few recorded cases of leprosy in which the portal of entry is probably known it may be inferred that disease begins with a primary lesion at the site of inoculation, and that this is followed by a lymphohematogenous spread. The result in the individual patient is largely dependent on his powers of resistance. Some patients impose little restraint on the bacilli and develop what is known as the lepromatous form of leprosy. Others, having a higher resistance, develop the tuberculoid form. In still others, a clear-cut type may not emerge until after a long time, if ever. These are said to suffer from an indeterminate type of leprosy. The differences between these general groups will be indicated below.

General systemic events. In general, leprosy is a disease accompanied by little or no toxicity. There are, however, events in the course of the disease known as reactions, during which the patient is acutely ill. In lepromatous leprosy the reaction is febrile and the patient is seriously and, at times, fatally ill. The tuberculoid reactions are charcterized by exacerbation of skin lesions and nurities. In both instances, the reactions suggest attempts at healing. In lepromatous leprosy the reaction is abortive, but in tuberculoid leprosy a reaction may actually be a good prognostic sign.

The skin lesions in leprosy are due to an actual bacterial dermatitis, whether localized or widespread. Lepromatous leprosy, in which the dermatitis is widespread, is unique among dermatitides in that billions of bacilli may exist in the skin in an almost saprophytic condition for a long time. As in any dermatitis, redness, heat, and swelling may be expected with the onset, with exacerbation, or with inflammatory response on the part of the host. The bacteria proliferate and the lesions grow in size as masses of bacilli are engulfed, but not destroyed, by phagocytic lepra cells. Visible, raisedt umefactions, known as lepromas, appear.

The more intense the inflammation, the redder the lesion. Ulceration may occur with extrusion of the focus. A change from a red to a brown color denotes declining activity, and ultimately the tumors become pale and flat, suggesting quiescence.

In tuberculoid leprosy, on the other hand, the patient, having a higher power of resistance, localizes the invading organisms from the start, and a single or a relatively few lesions result. Characteristically these are asymmetrical in distribution. A progressing lesion is more or less annular and presents a raised, nodular, active border and a flat, atrophic center.

The peripheral nervous system. ***Myc. leprae*** induces neuritis by invading and causing reaction in the connective tissue stroma of peripheral nerves. To this is due the clinically perceptible enlargement, best appreciated where a nerve trunk passes close to the surface over a solid substructure. The chief signs of the neuritis are anesthesia and lower motor neuron paralysis distal to the lesion. Severe neuralgia may occur during an inflammatory reaction. Marked nerve involvement can produce gross deformities, such as extensor paralysis of the fingers or facial paralysis. Such lesions are especially prominent in tuberculoid leprosy, but may occur to a lesser degree in the lepromatous type. They may leave the patient a cripple, unable to care for himself, long after he has ceased to be a menace to the public health.

The respiratory mucosa. In the nasal mucosa, ***Myco. leprae*** causes congestion with or without ulceration and nosebleed. From the nose the process may spread directly to the pharynx, larynx, and trachea. Exhaled bacilli are probably a source of infection. The breathing heard in nasal leprosy resembles that in hypertrophic rhinitis.

The lymphatics. Enlargement of the regional lymph nodes usually accompanies infection of the skin. The more general the infection, the more generalized the lymphadenopathy. The extent of lymph node enlargement noted in leprosy is roughly in proportion to the thoroughness of the physical examination. Lymphadenitis may obstruct drainge and cause ödema distal to the involved nodes.

Other clinical phenomena, which we have not observed, but which are not uncommon, are ophthalmitis, and testicular atrophy due to orchitis and accompanied by secondary eunuchoidism. In lepromatous leprosy bacterial invasion of the globe causes inflammatory destruction of the eye. In tuberculoid leprosy the eye may be damaged as a result of eyelid paralyses.

LABORATORY DATA

Ordinarily, the diagnosis of leprosy is made on the basis of the physical examination alone. Often, however, recourse is had to the laboratory for aid in differential diagnosis and in classification. The examinations made in our patients were nasal smears, dermal smears and biopsies. Roentgenograms may at times

define trophic bone changes. Other tests, such as urinalysis and blood count, are of use only when normal values are altered by complications, intercurrent disease, or therapeutic misadventure.

Nasal smear. Scrapings are taken from septal or turbinate lesions and stained for acid-fast bacilli. A positive result is not pathognomonic because tubercle bacilli or saprophytes may be found in the nose. Clumps of acid-fast bacilli arranged in bundles like cigars are, however, confirmatory evidence of a clinical diagnosis of leprosy.

Tissue smear. A slit is made in a suspected lesion and the juice smeared, or, preferably, a bit of tissue is excised and macerated on a slide. The finding of acid-fast bacilli in such a preparation can mean only leprosy, provided tuberculosis cutis and the new mycobacterial infection described by various authors can be eliminated.

Biopsy. A section of a skin lesion or of a lymph node is removed and stained for acid-fast bacilli and for histologic study. The presence of acid-fast bacilli has the same significance as their presence in a dermal smear. In the hematoxylin-eosin preparation, large foamy lepra cells are diagnostic of lepromatous leprosy. Epithelioid cells and tubercles, in the absence of tuberculosis cutis, mean tuberculoid leprosy. A general round-cell infiltration of the granuloma type, with neither lepra cells nor tubercles, is nonspecific, but supports a clinical diagnosis of uncharacteristic or indeterminate leprosy.

DIAGNOSIS

Leprosy is one of the most easily recognized of diseases provided its existence is not forgotten. There is nothing else which causes the combination of fixed dermatosis, peripheral neuritis and nasal obstruction, with or without lymphadenopathy and fever. Unfortunately, the most easily recognized case is the far-advanced case. The public health and clinical refinement demand earlier detection. To this end a suspicious-minded examiner and a painstaking physical examination are necessary because there is no known biologic or mechanical screening test. The procedures listed in table below should be followed as a matter of routine. Good illumination by sunlight is essential for observation of skin lesions.

These procedures are described as minimal because positive or suggestive findings will naturally lead to further investigations, such as anterior rhinoscopy or tests of sensation.

The differential diagnostic problems encountered in our patients included erythema multiforme, chronic ulcers and epistaxis.

Minimal physical examination for leprosy

Method	Area	For
Inspection	Face and ears	Thickening, redness, nodulation, atrophy, dermatosis, alopecia
	Neck (head rotated)	Enlarged auricular nerves
	Trunk and extremities	Dermatosis, erythema, ulcers, edema, enlarged nerve trunks
	Digits	Loss, ulceration, deformity
Palpation	Skin	Confirmation of visible lesions; subcutaneous nodules
	Lymph nodes	Lymphadenopathy
	Nerve trunks	Enlargement
Audition	Nose	Obstructed, noisy respiration

CLASSIFICATION

The classification of the type of leprosy in the individual patient is important from the point of view of prognosis and of the public health. A patient with minor lesions, containing a few bacilli and having a high natural resistance is evidently a good risk, whereas a patient with many lesions rich in bacilli and poor resistance is a poor risk.

The ideal method of classification is by means of the lepromin test. This intradermal reaction to killed lepra bacilli indicates the resistance of the patient, a strong reaction meaning strong resistance and no reaction poor resistance, corresponding respectively to the tuberculoid and the lepromatous forms of the disease. Unfortunately, an attempt to manufacture lepromin was unsuccessful, owing to lack of suitable material. Hence in our cases classification had to be based on clinical, bacteriologic and pathologic findings only. The chief considerations are shown in table below.

Nonimmunologic basis for classification of leprosy

Consideration	Lepromatous type	Tuberculoid type
Skin lesions	Symmetrical Nodular Center elevated Border not sharp	Asymmetrical Annular Border elevated Border well demarcated
Nerve lesions	Minor	Major
Bacilli on dermal smear or section	Abundant	Few or absent
Histology	Lepra cells	Tubercles and epithelioid cells

JOHN A. C. GRAY,

U. S. Armed Forces Medical Journal, Vol. III, No. 9, Sept. 1952, Pp. 1287.

Rectal Lymphogranuloma Venereum

My subject this afternoon is very comprehensive and I shall not summarize the historical background, as important as that phase is in comprehending a disease entity, but shall mention briefly those workers, truly outstanding, whose contributions represent milestones in our knowledge of the disease.

Mass surveys conducted by administering the Frei test to routine admissions at the Harlem Hospital and other large medical centers throughout the country having a mixed population, indicate that the disease has affected an unwarrantedly high proportion of the American population, with a predominance of the infection in Negroes. It is true that many of the ca es remain asymptomatic, but even these are a constant public health menace.

All centers report a very high incidence in female patients as against male in cases admitted with symptomatic lymphogranuloma venereum with its various manifestations and complications, especially with regard to the development of rectal stricture. In our studies the female cases comprised 82.9 per cent. This high incidence of symptomatic and active disease in women, so out of proportion to the findings in various surveys which report the incidence to be more predominant in males in asymptomatic patients, has been an interesting point of pathogenetic importance, one which has interested investigators for many years. It is generally agreed that, while the primary infection in women with rectal manifestations takes place in the vagina or cervix, primary infection in men in cases with rectal involvement is more likely to be the result of sodomy. With the initial infection in women being per vagina, why is it that the symptomatic disease in this sex shows itself overwhelmingly as rectal in its manifestation? Nesselrod demonstrated that in women the lymphatic drainage from the external genitalia is inguinal as in men, but that the drainage from the vagina and cervix is pelvic with interlocking channels to the perirectal area. This deduction was confirmed by other workers. Our observation has been that in male patients the disease manifests itself with an acute inguinal adenitis, progressing to bubo formation and on to an anorectal inflammatory process which gives off a sanguinopurulent exudate, often with the development of fistulas, with but few cases going through to stricture formation. The female cases have evidenced a predominance of stenotic changes in the rectum with stricture formation, as well as overlying inflammatory manifestations.

While most authors are of the opinion that a determining factor in the production of rectal stricture is a resultant disturbance in the lymphatic flow produced by the infection, some have tried to explain the development of stricture in the female on injury during childbirth and trauma secondary to vigorous coitus, as well as a greater tendency to ulcers in the rectum due to impacted faces in cases of constipation (usually more prevalent in women). Wright, Freeman

and Bolden, in their comprehensive resume of 476 cases of lymphogranulomatous strictures or the rectum, pointed out that trauma during childbirth cannot seriously be considered a major causative agent and stated further.

That lymphostasis plays an important part in the pathogenesis of rectal strictures in three ways: (1) blockage of lymph glands and interference with adequate drainage; (2) involvement of the lymph channels themselves, due to the action of the virus, and (3) a specific scar tissue-producing action of the virus.

Of all of the early workers striving to solve the many complexities of the disease, Dr. Henri Hartmann stands out. To him goes credit for recognizing seriousness of the disease and giving it careful and prolonged study in all of its surgical aspects. He foresaw the importance of excision of the rectal stenotic area in the eradication of the disease and worked to better technique and procedures for approximately forty years, dating back to the late '90s. He recognized the fact that fecal diverting colostomies, dilatations and simple procedures only give temporary relief and can in no manner take the place of radical surgery in advanced cases of rectal stricture. His articles and reported case histories are still outstanding despite the fact that he knew nothing about the Frei test, the true etiologic agent, or the systemic nature of the disease, which are of more recent date.

To Dr. Wilhelm Frei we owe much credit for advancing the studies of the etiologic factors of the disease. His intradermal test, reported in 1926, brought forward evidence which proved that the occurrence of benign strictures of the rectum and elephantiasis of the genitalia was of lymphogranulomatous origin. This stimulated studies which brought to light the wide-spread systemic manifestations of the disease.

Hellerstrom and Wassen, in 1930, by means of intracerebral inoculation of monkeys, proved that the disease was due to a filtrable virus. Today the virus is demonstrable microscopically and can be grown on chick embryo media.

In recent years the outstanding contributor to our knowledge of lymphogranuloma venereum has been Dr. Louis T. Wright. He correlated the pathological findings in the largest series of cases ever reported, thereby clarifying points of diagnostic and prognostic importance, previously somewhat nebulous. He believed with Hartmann that excision of the stenotic area offered the best chance for eradication of the disease in low rectal strictures. In 1926 he adapted the Victor Pauchet excision procedure to the surgical management of these cases. In this operation the external sphincter is preserved and the rectosigmoid proximal to the excised area brought down through the anal orifice. He very soundly used stage procedures. The first stage was a temporary, diverting colostomy, performed far enough ahead of the definitive excision procedure to correct the effects of chronic obstruction, permit secondary infection to subside

and bring about a restoration of normal weight as well as metabolic balance. This greatly enhanced the prospects of the definitive surgery which followed. Cases are not evaluated as to results until well after the colostomies are closed. In 1946 Wright et al reported 26 cases with highly satisfactory results with only 2 deaths, and these not directly attributable to the operation. This series has been enlarged since this initial report. This stimulated workers in other centers to adopt excision as the treatment of choice. Noteworthy was the fine series reported by Breidenbach and Slattery, in 1949, using a somewhat different approach, but with the same fundamental principles, namely, a stage procedure with a preliminary defunctioning colostomy.

It is to be emphasized that the late manifestations of lymphogranuloma venereum, such as benign strictures, extensive stenoses of the lower colon and rectum, chronic fistulous tracts, elephantiasis of the perineum, anal tags and tumors of the cockscomb type, all call for surgery, in some cases definitive, in others palliative. That surgery should not be neglected nor delayed beyond a reasonable time is emphasized by the increasing number of case reports of carcinoma superimposed upon granulomatous lesions. Pund and Lacy in 1951 reported 85 cases of penile, vulvar and anorectal carcinoma, 36 per cent of which had positive Frei tests, a condition not paralleled in other venereal diseases. They concluded that persistent lesions of lymphogranuloma venereum predispose to carcinoma.

In cases too extensive for local excision and restoration of continuity of bowel it may be necessary to resort to permanent colostomy and, if feasible, abdominoperineal resection.

It is in the effective management of the early cases of lymphogranuloma venereum that the eventual control and eradication lie. I speak of the cases which manifest a proctitis evidenced by an anal discharge of pus, mucus or blood, alone or in combination; those cases with early changes in bowel habits or size of the stool; and those cases which have perianal infection with multiple fistulas, often a rectovaginal fistula. I have in mind also the cases which evidence unilateral bubo formation. It is these and symptoms which call for a confirmatory Frei or complement fixation test and, at times, a biopsy.

Down through the years the failure of drug treatment of these early manifestations and the limited results from fecal diverting colostomy are known to all of us. Even in recent years the use of penicillin, streptomycin and the sulfa drugs gave improvement, limited apparently to the secondary invaders. The patients continued to progress to the late manifestations because the basic disease process due to the virus remained untouched. In our hands, and we tried a large series of cases on the sulfa derivatives, the immediate improvement did not stand up. Their virucidal action is still highly questioned and not proven.

The really startling upswing in the control of this infection and the treatment of the early lesions became an actuality when, in 1948, Wright and his co-workers reported the use of aureomycin for the first time in human beings. This new antibiotic was shown to possess high virucidal properties. Its use in human beings had been preceded by a comprehensive screening program at the producer's laboratories. It was noted that there was a striking spectrum of activity exhibited by this antibiotic against many rickettsiae and certain viruses, and that it was effective in the treatment of mice infected intracerebrally with the virus of lymphogranuloma venereum. The cases used in humans were those infected with lymphogranuloma venereum. A total of 25 cases was studied. The dosages used were far below those now realized as optimum, but even these limited dosages gave striking results. Eight of the 25 cases had buboes which showed a decided reduction in size of the nodes at the end of four days. Inclusion and elementary bodies characteristic of lymphogranuloma venereum obtained by aspiration before treatment were greatly reduced in forty-eight hours, and, by laboratory studies, had disappeared within one week following the institution of treatment.

Three patients with suppurative proctitis showed decided improvement, 2 after a few days and the other after eight days of treatment. Proctoscopic examination at the end of treatment showed a normal rectal mucosa. Fourteen cases of benign rectal stricture due to lymphogranuloma venereum were studied and, while they evidenced no gross pathologic changes in the fibrous rectal stricture, they had a decided decrease in rectal pain, discharge and bleeding, with an increase in the size of the stool. We feel that surgery only will correct the fibrous stricture. In the meantime the superimposed active virus infection with secondary invasion can be eradicated.

We have handled many cases with aureomycin, terramycin and chloromycetin, with ever increasing excellent results. No cases, once thoroughly treated, have so far gone through to stricture formation or other late manifestations. It is our belief that the virucidal properties of these new antibiotics have given use the answer with regard to the treatment of this disease, namely, that treated cases will not develop the late sequelae if seen early enough and treatment is thorough. We feel that even the late cases will be improved as regards the overlying active infection.

The optimum dosage of the drugs is one gram a day divided into doses of 250 mg. each. The duration of treatment varies from two to six weeks depending upon the type of pathology, the action of the particular strain and the immunity reaction of the host. Treatment is shorter in bubo and proctitis, and lengthens in the management of the more chronic stages which evidence fibrosis or fistula. Recurrence usually indicates inadequate therapy and a second course should be

instituted. In our hands the Frei test, positive at the beginning of treatment, is not changed.

We have also used the drugs in suppository from with rapid improvement in the condition of the mucous membrane, alleviation of anorectal paid and itching, and increase in the circumference of the stool.

With the simple diagnostic armamentarium of the Frei test, routine digital anorectal examinations and the anoscope, along with an occasional biopsy when lesions are suspicious of carcinoma, you can save your patients much trouble in later years and even appreciably reduce the incidence of this disease in your communities by the yearly and thorough use of these drugs.

In conclusion, let me emphasize that is our firm belief, based upon a large series of controlled cases, that the newer antibiotic drugs, aureomycin, terramycin and chloromycetin, are highly effective virucidal agents in the treatment of lymphogranuloma venereum in its early manifestations. It is our feeling that surgery is indicated once fibrotic changes, representative of late manifestations have taken place. Finally, it is our opinion that, even in late cases the drugs are effective adjuncts to definitive surgery.

ROBERT S. WILKINSON, M. D.

—*The Harlem Hospital Bulletin, Vol. 5, No. 3, Dec. 1952, Pp. 75.*

Some Aspects of Therapy of Sweat Disturbances

The Clinical importance of disturbances in sweating is being more and more widely recognized. It has become apparent that the sequelae of such disturbances are responsible for a variety of cutaneous and systemic disorders. The object of this paper is to review briefly some of the available therapeutic measures in relation to the following three categories of sweat disturbances:

I. Hypohidrosis or anhidrosis.

II. Hyperhidrosis.

III. Dyshidrosis or pathidrosis, i. e. abnormal composition of the sweat, or conditions in which both preceding quantitative disturbances are combined or in which one of the two quantitative disturbaces coincides with some other disorder or disocders.

I. THERAPEUTIC MEASURES IN HYPOHIDROSIS OR ANHIDROSIS

Whether the hypohidrosis is functional or due to structural changes in the sweat organ, general measures, such as reduced fluid-intake, rest, and protection from environmental heat and high relative humidity, are likely to prove useful.

Climate and Climatized Rooms.—The spectacular improvement in many anhidrotic and dyshidrotic conditions and the relief afforded in severe and otherwise intractable forms of the sweat-retention syndrome after transfer of the patient

to geographic areas with a more favorable climate illustrate the importance of environmental climatic conditions in relation to many sweat disturbances.

In view of our present concepts of the pathogenetic mechanisms of the sweat-retention syndrome, it is logical to suggest the transfer of the patients to completely air-conditioned or climatized rooms, where controlled atmospheric conditions and deliberate lowering of the relative humidity facilitate evaporation and, thereby, the dissipation of heat form the body. The studies of Sulzberger and Emik on Guam, for example, showed that incidence of prickly heat could be reduced by nearly 50% when 8 duty hours of every 24 were spent in climatized rooms.

Artificially Induced Sweating and Facilitated Evaporation.—In various conditions which obstruction of the sweat ducts is either the underlying or a contributory factor, exposure to dry heat and subsequently facilitated evaporation have been found useful.

The procedure is carried out as follows: A reflector-type sweat box with incandescent light bulbs is placed over the trunk of the patient, who must be completely naked. The lights are turned off as soon as sweat droplets are visible. The patient should remain uncovered with limbs in maximal abduction until the sweat has completely evaporated. This procedure has been found to benefit a number of patients suffering from atopic dermatitis aggravated by sweat retention, those with lichenoid eruptions caused by sweat retention, and even some patients having lichen planus. The treatment should be repeated once daily at least, for as many weeks as appear necessary. For the time being, it is assumed that relief afforded by this procedure may depend to a significant extent on a forcible expulsion of plugs from the sweat ducts by the increased flow of sweat.

Vitamin A.—We have long been favorably impressed by the effect of large doses of vitamin A (50,000 units of aqueous vitamin A daily for several months) in some patients with horny plugging of the sweat pores and the signs of sweat retention. The effect perhaps is due to softening of the keratin, leading to decreased formation of horny plugs and loosening of those already present.

Hormones.—When imbalance of endocrine function is suspected of playing a substantial role in the disturbances, endocrine and metabolic studies are indicated, with subsequent administration of suitable hormones, such as thyroid hormones, androgenic steroids, or corticosteroids.

Sodium Salts.—It appears advisable to restrict the intake of sodium salts in serious anhidrosis. Link, Peperhowe, Kuno, Ito and Kosuge, Nishibori Kashiwabara, and others observed that sweat delivery after exposure to heat or upon physical exertion was significantly retarded and reduced after oral or intravenous administration of sufficient amounts of sodium chloride. That a reduction in the intake of sodium chloride combined with an increased water intake produces

a beneficial effect upon miliaria was demonstrated clinically by Horne and Mole and other British investigators, who showed that specifically sodium may be responsible for the production or aggravation of prickly heat. When, instead of such salts as either sodium chloride or sodium dihydrogen phosphate or sodium citrate, ammonium chloride was administered, no comparable deleterious effect was observed.

Topical Application of Drugs Stimulating the Autonomic Nervous System.—Increased sweating may be induced not only by the systemic but also by the topical application of drugs stimulating the autonomic nervous system. Representative of these are pilocarpine, acetylcholine, and, as shown by both earlier and more recent studies epinephrine. To induce this effect in situ, these drugs may be injected intracutaneously or applied electrophoretically; the effects, however, are so transitory as to limit the practical value of the methods.

Similarly, external application of 2,4-hexadien-l-ol (hexene-ol) will noticeably increase thermal sweat delivery in any skin area, but the stimulating action is too brief to be of much promise in therapy.

Topical Application of Hydrophilic Fats.—Increased sweat delivery on the application of wool fat (lanolin) was described by Unna, Wolpert, and Rothman, and more recently confirmed by O' Brien, who obtained a similar effect with several other lipids. Our experimental findings, after the application of wool fat and other hydrophilic ointments and waxes, were substantially the same as those of previous observers. However, these agents were hardly of any clinical use in the treatment of patients with sweat retention.

Peeling Procedures.—Peeling, induced, for example by the application of sali-cylic acid (3 to 10% solution in alcohol) or by exposure to ultraviolet rays, may facilitate sweat delivery. Utmost caution is urged in the use of such procedures, since they result in an accumulation of horny material at the sweat pores and a consequent aggravation of the sweat-retention syndrome.

II. THERAPEUTIC MEASURES IN HYPERHIDROSIS

It is important at the outset to differentiate between *emotioal* and *thermal* hyperhidrosis, since in each case the basic mechanisms are different. Obviously, emotional hyperhidrosis is likely to improve with avoidance of mental and emotional strain, while thermal hyperhidrosis will respond to limitation of physical activity and protection from environmental heat and high relative humidity. Nevertheless, as a general rule, rest is of great benefit in any and all forms of hyperhidrosis. Restriction in the intake of fluids will, understandably, somewhat reduce the quantities of sweat. But a practical application of any of these principles is difficult.

Anticholinergic Drugs.—*A.* Systemic Application: The systemic use of the "classic" anticholinergic drugs, atropine and scopolamine, or of such drugs

as homatropine and adiphenine (trasentine; 2-diethylaminoethyl diphenylacetate) hydrochloride is severely limited because of their toxic effects and the relatively short periods of relief they afford. It has been established by Shelley and Horvath that a large oral dose of atropine will significantly inhibit sweating (locally induced by topical administration of pilocarpine at different intervals over a given period) for 30 minutes after its administration, but that after another 30 minutes this action is already at an end. These drugs are best administered, therefore, for relatively short periods and on occasions when they may be of decisive value, as, for instance, during attacks of grave sweat-retention syndrome, or prior to anticipated mental stress in emotional hyperhidrosis, or to forestall acute exacerbations in intertriginous areas or on the hands and feet in hyperhidrosis complicated by dyshidrosis.

During the past year, the new anticholinergic compounds methantheline (banthine) bromide and diphenmethanil ("prantal") methylsulfate have been recommended as suitable for prolonged systemic use, chiefly because of an asserted low incidence of side-effects.

Recently, Brown and Sandler obtained encouraging results with methantheline in the treatment of hyperhidrosis, intertrigo, and eruptions of the hands and feet related to disturbances in sweating. Therapeutic amounts of the drug (100 to 200 mg. daily given over an average period of eight weeks) gave rise to initial dryness of the mouth in seven, transient disturbances in ocular accommodation in three, and transitory urinary retention in one of the subjects.

Nelson observed a good response to diphenmethanil in one patient in whom methantheline had failed, whereas methantheline helped two patients who had not responded to diphenmethanil. In two patients neither methantheline nor diphenmethanil was found to be of benefit. With the exception of headaches, which occured in one patient whenever diphenmethanil was administered, no side-effects were observed from this drug.

Our experience with these drugs has so far been too limited to permit an evaluation. Only one of seven patients we treated with methantheline (four to six times 50 mg. daily for periods of one to four weeks) showed some decrease in hyperhidrosis after three weeks, while five complained of dryness of the mouth. Of six hyperhidrotic patients receiving diphedmethanil (four to eight times 50 mg. daily for a period of one to four weeks) two appeared to benefit from the higher doses. Possibly our dosage was too small for the other patients, or the periods of administration of the drugs were too short; we are therefore, carrying out more extensive trials with different dosage schedules. In any case, methantheline, in addition to urinary retention and other ill-effects already mentioned, may produce vertigo, salivary oppression, constipation, general weakness, etc.

B. Topical Applications: According to Shelley and Horvath, a single local application of a 1% aqueous solution of scopolamine hydrobromide to

hyperhidrotic areas for about 10 minutes can distinctly sweating for a period of five to eight days. The striking experimental results obtained by these investigators indicate that scopolamine hydrobromide (as well as atropine methyl nitrate and atropine sulfate, which are only slightly less effective) may prove to have some therapeutic significance in the treatment of severe forms of hyperhidrosis. The topical application of scopolamine hydrobromide is definitely contraindicated if dermatitis is present, as toxic amounts of the drug may be absorbed. Unfortunately, the application of these solutions to hyperhidrotic palms and soles appears to be impractical, since absorption is insufficient in these areas.

General Sedatives.—Patients with hyperhidrotic conditions, especially emotional hyperhidrosis, often respond to general sedatives, such as barbiturates in low dosage, bromides (e. g., calcium bromidogalactogluconate [calcibronat]), or tincture of valerian. As a rule, these sedatives are better tolerated than the anticholinergic alkaloids and are of special value whenever medication over a long period is desirable.

Antihistaminic Drugs.—The report on an "acetylcholine blocking effect" of antihistaminics by Perry, Hosmer, and Sternberg and the discussion of this report by Cornbleet, Rothman, and Andrews encouraged us to try tripelennamine (pyribenzamine) and diphenhydramine (benadryl). Thus far, the results in both emotional and thermal hyperhidrosis have not been promising.

Roentgen Rays.—The application of roentgen rays to hyper-hidrotic skin areas is considered useful by most experienced dermatologists, in particular by MacKee, who obtained some of the earliest favorable results with carefully administered doses. Miescher and Boehm recommended divided doses to a total of 1,100 to 1,600 r, with 100 kv., 2 mm. Al filter, and a distance of 30 to 40 cm. This treatment was particularly successful when the hyperhidrosis was continuous rather than intermittent. Needless to say, the application of x-rays to combat hyperhidrosis calls for great skill and caution, since some kind of damage to the sweat organ is apparently responsible for the beneficial effect.

Astringents.—The number of astringent chemicals which are applied externally to counteract excessive sweating, is almost unlimited. As a rule, remedies which are not in some way and to some degree harmful to the skin tissues, either as nonspecific irritants or a potential sensitizers, do not appreciably alleviate hyperhidrosis.

Aqueous solutions of boric acid, resorcinol, potassium permanganate, lead acetate, aluminum subacetate, or tannic acid when applied to hyperhidrotic areas by means of compresses are effective and relatively safe in use. Such treatment, though inconvenient in execution, is of particular value in hyperhidrotic conditions of the hands and feet. It should be mentioned that the more active of these solutions, namely, lead acetate, aluminum subacetate, and notably tannic acid,

are potentially irritating to the tissues. Irritation is likely to occur when, as a result of rapid dehydration caused by the astringent, inflammatory exudate or sweat is retained under the altered tissue material. For this reason, solutions of these astringents must, as a rule, be applied for short periods only (about one to two hours daily), and, if continuous application is desired, it should be undertaken under strict supervision.

For applications by patting or dabbing, the choice of a mild or of a strong astringent solution will depend on the severity of the condition and the extent of any irritation already present. Examples of the milder solutions are tannic acid, 1 to 2% in alcohol or glycerin, and potassium permanganate, 1:5,000 to 1:10,000 in water. Formaldehyde, 5 to 10% solution in water or alcohol, is an example of a more effective, but also more potentially damaging, remedy of this type.

Electropositive Agents.—In view of the presumptive existence of an electrophysiologic potential along the sweat ducts, with electronegativity at the terminal portion, as demonstrated by a selective affinity of the spiral part for electropositive dyes, clinical trials with "dabbed-on" applications of water solutions of the quaternary ammonium base benzalkonium (zephiran) chloride (0.1 to 5%) and lithium iodide (10%) have been inaugurated most recently. Although several patients showed some reduction in hyperhidrosis, it is as yet too early to venture an opinion concerning the possible practical value of these solutions. It is strongly recommended that at the beginning of treatment with benzalkonium chloride high dilutions be used and the patient be carefully observed, as this drug may induce primary irritation, as well as sweat-retention vesicles.

Application of Galvanic Current and Electrophoresis.—The postulated electrophysiologic potential along the sweat ducts may also be reduced by means of a galvance current applied to the skin. We feel that this procedure may be tried particularly in the treatment of patients with emotional hyperhidrosis, rather than in that of patients with thermal hyperhidrosis, since in our experience the latter are more inclined to inflammatory complications from sweat retention.

Cataphoretic applications of aqueous solutions of formaldehyde to hyperhidrotic skin areas were recommended by Ichihashi. He reported that one series of three to four applications "could stop the suffering entirely at least for 1½ months, sometimes longer than 2 months." Good results were obtained on the palms and soles with a 7.5 to 10% solution of formaldehyde, applied under the anode with a current of 0.33 to 0.5 ma. per square centimeter for 10 minutes; in the axillae, however, a 5 to 7.5% formaldehyde solution and a current of 0.25 to 0.33 ma., applied for five minutes, were necessary for good results. Each course of treatment consisted of a total of three or four applications, given at intervals of about two days.

Ointments.—Of the many ointments employed in hyperhidrotic conditions, the old and proved unguentum diachylon album Hebra (lead oleate ointment) still

holds its place, especially in the treatment of exfoliating processes of the palms and soles. Dressings with the ointment are applied overnight or, when feasible, are changed only once in every 24 hours. Hopkins and his group recommended polyethyene glycol (carbowax) with 10 to 20% powdered tannic acid for this purpose.

Antiperspirants in the Axillae.—In discussing the many antiperspirant creams, solutions, and other preparations in use to reduce axillary sweating, we shall confine ourselves to a very brief reference to probable principles of their actions. Experiments with preparations containing aluminum salts have shown that these salts affect eccrine and apocrine glands differently, damaging the ducts in the former and the glandular epithelium in the latter. Our studies suggest that the epithelium of the apocrine glands is more readily damaged by locally applied antiperspirants than are the ducts of the eccrine glands. This would explain our observation that antiperspirant preparations are much more effective in the axillary vaults than in other skin areas where only eccrine glands are present. Moreover, since a relatively weak influence is capable of sufficiently damaging the apocrine epithelium to reduce sweating without causing ductal or periductal changes, the relatively rare occurrence of papulovesicular and consequent pyodermic eruptions on application of antiperspirant products to the axillae can be more readily understood. In our experience, certain persons are especially inclined to show this eruptive form of sweat retention in response to practically any antiperspirant, and this inclination may be shared by members of the same family. In any and all persons, unnecessarily frequent application of antiperspirants to the armpits is inadvisable. Persons habitually using an antiperspirant should individually ascertain the longest possible interval between applications which still permits the maintenance of the desired effect. In many instances one or two applications a week are entirely adequate.

III THERAPEUTIC MEASURES IN DYSHIDROSIS

Maintenance or Repair of Acidification.—Exposure to Dry Heat: Whenever dyshidrotic conditions are complicated by, or associated with, hyperhidrosis or anhidrosis or a combination of the two disorders, the general measures discussed previously may be applied. A large category of dyshidrotic conditions is characterized by a predilection for inteririginous sites, by stagnation of sweat because of inadequate evaporation, by maceration of the skin, and by a defect in the so-called physiologic acid mantle of the skin because of a shift in pH toward alkalinity. In these, the previously described treatment by exposure to dry heat and promotion of free evaporation from the skin surface may by helpful. With the aid of a few minor technical devices, such as insertion of cork wedges between the distal parts of the toes, we have obtained favorable results with the heating procedure in a number of patients with intertriginous dyshidrosis.

Ventilated Footgear: It is certainly of great practical importance to support as far as possible the natural process of evaporation which maintatins dryness

and acidification of the skin surface. For this reason, subjects with dyshidrosis of the feet should preferably wear sandals, perforated shoes, or other types of "ventilated" footgear dur ng the summer.

Topical Agents: The simplest of the innumerable topical measures in use in the treatment of dishidrotic conditions–though often underestimated–still appear to be the most effective. This applies, for example, to bathing in dilute solutions of potassium permanganate, to keeping the involved areas completely dry by careful use of soft towels, and to the regular application of powder.

During the last 12 yea-s, Peck and collaborators, Rothman and his group, and others have clarified the nature of the action of the fatty acids or their salts, which contribute largely to the physiologic resistance of the skin surface to fungous infection. Even before these experiments Marchionini recommended the application of dilute hydrochloric acid, a buffer mixture containing lactic acid, or powdered boric acid to the dyshidrotic area. At present, powders containing undecylenic acid, propionic acid, or caprylate combinations are being used to combat or prevent secondary infection by fungi or bacteria. Sulzberger, Shaw, and Kanof showed that an undecylenic acid-zinc undecylenate powder has significant value in preventing common forms of cutaneous foot trouble in military personnel.

As an essential support of free evaporation from intertriginous dyshidrotic areas, where moisture and alkaline decomposition are apt to aggravate the condition, it is strongly recommended that all affected sites be treated by systematic applications of gauze strips sprinkled with powder. Patients with maceration or a tendency to maceration between the toes, for example, should insert powdered strips of gauze in the interdigital spaces every morning.

For the same reasons, deformities which interfere with the physiologic process of evaporation, such as flat and superimposed toes, should be corrected, whenever feasible.

HERRMANN AND SULZBERGER,
A. M. A. Archives of Dermatology and Shphilology,
Vol. 66, No. 2, Aug. 1952, pp. 162.

Genital Studies on Skin Disease (Hair Nevus)

In 1924, hair nevus was first described by Fessler under the name of congenital hair tumor as one kind of the teratomas and the second was reported by Nomura in authors' clinic (1938). Since that time, the reports of similar cases in Japan were presented by Yamaguchi-Kuroda and Momose (5 cases). The authors experienced recently two cases of hair nevus and studied especially on the condition of the nerves in the tumor with Bielschowsky-Seto's silver impregnation method.

REPORT OF CASES

Case 1. A 16 years old boy. No similar tumor was found in his families. Examination: There were 3 scallionlike soyabean-sized hard tumor on the frontal region of both tragi (two in the right and one in the left side) and their surface was covered by normal skin.

Case 2. A 9 months old male. His mother stated that his paternal grandmother had a similar tumor in the front of her left tragus which was removed in her childhood and that paternal grandmother's mother had also presented soyabeen-sized dark tumor on her right upper eyelid. Examination: There was a scallionlike peasized hard tumor on the frontal region of the left tragus and it was covered by normal skin with rosy tone.

Histological findings. The tumors in both cases are solid and decked by the normal epidermis. Extending from subpapillar layer to subcuits numerous hair follicles are found in various forms from embryo bud to fully developed one. Most of them, which situate in stratum reticulare, present variously sized cross sections but regular direction of the length axes. Some of them near the epidermis show the longitudinal section and a few of them reach to the skin surface showing normal downy hair. Other some hair follicles are accompanied by the sebaceous gland. In the other hair roots, several holes are found. These holes are equal to what Fessler described under the name of "Gemeinsame aussere Wurzelscheide mehrerer Haare" (Momose, 1949). But all of hair roots have never the arrector pili muscles and no sweat glands are found anywhere. In the second case, the subcutaneous fat tissue is comparatively well developed and the netlike connective tissue penetrates into it. In our first case, the cartilage is found in the deeper part of the tumor. Both cases present no figure of the invation of the epidermis as reported by Fessler.

Examination by Bielschowsky-Seto's silver impregnation method. The authors observed the relation between the tumor and the nerves with the Bielschowsky-Seto's silver impregnation method. The nerves are found around the blood vesseles or the hair follicles. Many sensible and fein vegetative nerve bundles run parallelly with the course of blood vesseles. The nerve bundles along the blood vesseles ramify for the hair follicles on this way. The ramified nerve bundles reach to the lower part or the sides of the hair follicles and advance upwards or down around the hair root. Viz. these nerve fibrers run in all directions and sometimes surround semicircularly the hair root. In some cases the nerve fibers look as if they surround circularly all round of the hair root from both sides. Many nerve fibers are generally found in the region between the hair follicle and the sebaceous gland. Even when the relation between the nerves around the hair roots and the blood vesseles cannot be found so clearly, the blood vesseles can more or less be found around the hair follicles and many nerve bundles run along them. And then the nerve bundles around the hair root

present the findings as follows. In some cases, a ramified nerve bundle reaches to the centre of the hair root. In other cases, some nerve fibers run to the hair root parallelly each other or enter radially from all round of the hair root.

These nerve bundles show no abnormal findings as hypertrophy or fissure and a certain relation between the degree of growth of each hair follicle and the number of nerve bundles around it can't be recognized.

COMMENT

Hair nevus has been already discussed by Fessler, Nomura, Yamaguchi-Kuroda and Momose.

The existence of the cartilage in the tumor was already reported by both Fessler and Momose. The similar finding was found also in our first case. The sweat glands which had been found in the cases by Fessler and Nomura were not present in the cases by Momose and us, while the sebaceous glands were seen more or less in all reports. Fessler and Nomura found the slightly developed subcutaneous fat tissue, but Momose did not recognize them. In our second case, the comparatively well developed subcutaneous fat tissue could be found.

The authors could find no reports in the literature in which the relation between the tumor tissue and the nerves was observed. Seto stated the distributional cource of the nerves in the head skin as follows. "The nerve bundles in the head skin start from the thick bundles in the aponeurosis as the mixed nerves and run upward in the interlobular connective tissue of the subcutis. First of all, they make the primary nervous plexus in the zone where the sweat glands are situated and this plexus combine with the plexus of the vegetative nerves around the blood vesseles. Then they run for the papillary upwards along the arrector pili muscles and make the secondary nervous plexus in the subpapillary. On the way, they give the branches to the hair follicles and these nerve bundles reach to the neuroshell in the follicle neck running horizontally between the arrector pili muscle and the basis of the sebaceous gland, and there ramify to fein fibers. In this part the hair nerve fibers make the end aparatus. On the other hand, the vegetative nerve bundles are rich around the blood vesseles and run along them. They are also rich around the sebaceous glands, the hair follicles and the arrector pili muscles." In our two cases, the course and the distribution of the nerve could not be observed in detail as Seto. The neuroshell in the neck of the hair follicle also could not be found. But it is guessed that the area, where the nerve bundles around the hair roots could be found, agreed with the neuroshell described by Seto. Many nerve bundles around or along the blood vesseles also could be found. Thus the fact that the nerve bundles are very abundant around the hair follicles was recognized.

Prinz described that the development of hair nevus is based on the abnormal growth of the epidermis as the invation of the epidermis reported by Fessler. But no figure as he described could be recognized in our two cases.

It stated as follows: "The inheritance on the supernumerary ears or the cartilaginous nevus was recognized by Siemens, Thomas, Rohrer, Hunt, Brander, Jenkins, Teveli, Miller and Miller, Ono, Hara, etc. Then it was able to presume that the hair nevus also is inheritable, although there had had no favorable report." In second case the grandmother was removed from the scallionlike soyabean-sized tumor in her childhood, and it gives some sugestion to Ito's presumption.

—M. MIURA AND A. KOMATSU,
The Tohoku Jn. of Expt Meaicine,
Vol. 56, No. 4, 1952, Pp. 352, Tokyo.

INTERNATIONAL PROGRESS IN COMBATING V. D. & DERMATOLOGY

Voluntary Reporting of Venereal Diseases

A central registry of venereal disease cases and contacts was established in 1944 in the Illinois Department of Public Health to elimmate duplication of reportiag and to provide a screening device for laboratory positives, field assignments, and correspondence. All information pertinent to the case or contact is coded on punch cards and filed alphabetically with this registry. A duplicate set of cards containing morbidity data is kept for background.

Records in this central registry show that some individuals are reported repeatedly for clinical progression in the course of syphilis, as new infections of syphilis, and as new infections of gonorrhea. This information, when filed in a central registry, provides an instrument which lends itself to analysis of administrative procedures. It is also proposed to use this method to determine whether contacts to primary or secondary syphilis cases who had been found upon initial examination to be not infected would, because of their presumed promiscuity, be reported subsequently as new cases of venereal disease. With the results of such a study in mind, efforts might be directed toward subsequent programs to follow up these contacts to primary and secondary syphilis cases, in an effort to find new cases of venereal disease.

Such a study suggests two avenues of approach: (*a*) a check of the central registry to determine voluntary reporting of such contacts as cases by private physicians or clinics, and (*b*) an actual field demonstration on contacts found previously noninfected. This paper is based upon the first method.

METHOD

Since the establishment of an assignment and report form in 1944, all information on each case followed as a field assignment is recorded on a punch card, making possible the tabulation in the central registry of results and other pertinent data on venereal disease investigations. For this study, all reports of contact investigations in which information was available on contacts to primary

and secondary syphilis cases were sorted from the file. The reports which indicated that the contact was not infected when examined were used in this study. A list of such contacts to primary and secondary syphilis cases who were found upon investigation to be not infected was established for each year from 1946 through 1950. Records on these contacts, giving pertinent information, such as age, sex, color, and county of residence, were filed alphabetically. The records were then checked against the central registry files for any diagnostic and treatment data availabe there. In some cases, central registry information represented data obtained prior to completion of the original investigation; in most cases, after the completion of the original investigation.

DISCUSSION

This study indicates that of the 1,935 contacts checked, 90, or 4.6 percent, were subsequently reported as cases of syphilis. Of the syphilis cases found, 59 per cent were diagnosed as being in the primary and secondary stages. It is interesting to note that most of these infectious cases were diagnosed during the first year after they were examined as contacts and found to be not infected. In order to determine whether any of these infectious cases were missed during their initial investigation and examination as contacts, a sample survey of similar assignments indicated that the notation "examined not infected" was entered on these investigation reports at varying lengths of time after the exposure date–70 percent were followed for 90 or more days; 20 percent, 60 to 90 days; and 10 percent less than 60 days. If this sample is acceptable as representative of the whole experience, the number of contacts subsequently reported as infected, and probably by the same initial exposure, would be insignificant. It must be remembered that 10 percent of the cases were followed less than 60 days–an interval well above the average incubation period for the disease. This, however, does not minimize the need for adequate follow-up of such contacts.

The percent of cases (4.6) subsequently reported among contacts initially found noninfected is deemed to be significant in view of the fact that these were spontaneously reported without added follow-up incentive. Compared to the rate of voluntary reporting of new cases among the population at large, this group of contacts, who have been at risk and may continue to be at risk because of established promiscuity, constitutes a reservoir of new cases toward which case-finding efforts might be directed. The statistics which in recent years have pointed out the magnitude of undiagnosed, and hence unreported, cases tempt the inference that many more new cases could be elicited by re-examining the "noninfected-contact" reservoir, for in it there may well be many subsequent exposures. Certainly, serologic surveys are not selective of such groups but are applied to the general adult population at great cost and extremely low yields of early infectious cases.

With prolongation of time for presumed promiscuity, when all other factors are constant, increased cumulative exposure, and hence increased infection and

subsequent higher incidence of voluntary reporting are expected. Certain factors which qualify these assumptions are: (*a*) the increased incidence of venereal disease during war periods, and (*b*) the present decreasing incidence of reported new infections of venereal disease. In this 5-year study, representing a period of national emergency after the termination of World War II, the reported infection rate of syphilis rose and then declined preceipitously. During the peak years of infectivity, increased promiscuity probably yielded increased morbidity because of increased exposure risk, while during the years of decreasing infecti vity, promiscuity may not have yielded similar increased mobidity because of the lesening of this risk.

The entire yield of the investigation of contacts to infectious cases of syphilis who were found not infected on their initial examinations will be determined not only from spontaneous reporting of such contacts as new cases of venereal disease, but also from a careful field investigation of such contacts who were not spontaneously reported. It can, however, be noted from results of this study that a follow-up of a presumed promiscuous population may be worthy of administrative trial, inasmuch as cases reported voluntarily represent only those who seek medical care from physicians who may not report them to a health department. Such an approach is now in operation on a demonstration and research basis and will be reported later.

SUMMARY AND CONCLUSIONS

1. Of 1,935 contacts reported after investigation as noninfected; 266, or 13.7 percent, were subsequently reported as having become infected with syphilis or gonorrhea. Of these, 198, or 10.2 percent, of the contacts initially investigated were found infected sometime after the conclusion of the initial investigation.

2. Syphilis cases reported in this group totaled 90, or 4.6 percent. of all noninfected contacts.

3. Early infectious (primary and secondary) syphilis totaled 53 cases, or 58.9 percent of all cases of syphilis subsequently reported.

4. The majority of all venereal disease cases subsequently reported among such "noninfected" contacts were reported within 1 year after the initial investigation.

5. The spontaneity of this reporting is emphasized and inferences drawn as to yield after re-examination of the noninfected-contact reservoir.

6. Voluntary reporting of venereal diseases by reporting agencies to the venereal disease central registry in the Illinois Department of Public Health has been utilized in this study to pinpoint administratively the need for further control measures in the follow-up of contacts to primary and secondary cases of syphilis, who, upon their initial examination and investigation, were found to be not infected with a venereal disease.

—By B. H. Sklar, L. M. Schuman & N. J. Rose of Illinois Dept of Public Health thro. Public Health Reports, Aug. 1952, Pp. 781. U. S. A.

First Victories Against the Loathsome Disease of Yaws

Yaws begins as a small insignificant sore on the foot or leg, a sore which grows and as the disease develops fresh sores break out anew elsewhere. The disease attacks the bones and eats away the tissues like termites, undermining the strongest physiques. The face may lose all human aspect and become nothing more than a nightmarish mask worthy of the legends of the Middle Ages.

These are the effects of yaws (also known as framboesia) which ravages the tropical regions of Africa, America, Oceania and Asia.

Particularly interesting revelations were made during a conference organized at Bangkok by the World Health Organization in collaboration with the Government of Thailand. The conference was attended by UNICEF representatives and outstanding specialists in yaws and treponemal diseases.

WHAT IS YAWS?

The contagious disease of yaws has for a long time been confused with syphilis. Both diseases are caused by identical micro-organisms, or treponemes, i.e. *T. pallidum* in the case of syphilis and *T pertenue* in that of yaws. Bejel, another treponemal disease, is prevalent above all in the Eastern Mediterranean area. The climate most favourable to yaws is a humid tropical one, where intense heat alternating with heavy rain, falls on a soil which is not very porous and gives rise to a luxuriant vegetation. It has been found that yaws tends to decrease during the dry season and to increase during the wet season. Primarily a rural disease, yaws is transmitted by human contract as well as by contact with dirty linen or clothing and other articles of everyday use. No decision has yet been reached as to whether insects act as vectors of the disease (flies, mosquitoes, etc.).

Undernourished individuals living in overpopulated areas are much more receptive than others. Peasants who move about barefoot in tropical countries are prone to develop foot lesions; the same phenomenon being noted amongst soldiers during the second world war.

It is extremely difficult to discover, before the characteristic lesions appear, whether a patient is suffering from syphilis or from yaws. Yaws itself is not hereditary, but a child born healthy to infected parents will in turn be infected by contact with them during infancy.

YAWS CAN BE CONQUERED

In the impressive Sahathai Hall of the grand palace of Bangkok, with its apparently jewel-encrusted prangs pointing to the sky, the King of Thailand had put several rooms at the disposal of those attending the conference. There, shirt-sleeved doctors, selected experts from all over the world, compared the results obtained in the control of yaws by the different international teams, including those of WHO.

The conviction rapidly grew that yaws could be definitely cured by giving the patients one, or at the most two or three intramuscular injections of repository penicillin at intervals of a few days. No tendency of the treponeme to develop resistance was noted.

Such treatment has proved more effective, less dangerous, cheaper and more manageable than all treatment with orally administered antibiotics, which must be preserved with for a longer time by patients who, despite the serious nature of the disease, often tend to forget medical advice all too quickly.

It should be noted that the majority of patients prefer to undergo injections, sometimes painful ones, rather than swallow other remedies, such as pills, etc., perhaps in accordance with the theory that " something that doesn't hurt cannot do any good."

Up to 31 December 1952, nearly 8 million persons had been examined in Haiti, Indonesia, Thailand and the Philippines, during the large-scale campaigns against yaws undertaken with the assistance of WHO and UNICEF; some 3 million were found affected and have been treated.

	Examined	Treated
Haiti	2,270,051	2,270,051
Indonesia	3,529,851	553,587
Thailand	1,679,342	216,047
Philippines	415,000	24,000

It has been calculated that the cost of the treatment given, including expenditure on staff and material, amounts to less than 3 dollars per head. Thus only 3 dollars may be the price of health and vigour in countries where the community needs an ever-increasing number of workers to improve its lot.

—R. R. Willcox, London Thro' WHO Press Release, New Delhi.

New Developments on the Leprosy Front

(The following is based on information received from WHO Headquarters in Geneva)

If we wish to stamp out leprosy, we must cease to treat leprosy sufferers as outcasts. Leprosy is infinitely less contagious than tuberculosis.

New drugs, which can be taken by mouth in the form of tablets, have proved highly effective.

BCG vaccination, whose role in the prevention of tuberculosis is well-known, may prove to have the same properties as regards leprosy.

Such are the four main ideas which emerged during the meeting of the first WHO Expert Committee on Leprosy, which took place recently at Rio de Janeiro and Sao Paulo in South America.

Leprosy, a disease prevalent from antiquity, still represents a very serious problem in the world today, the figure of 7 million sufferers being considered as lower than the actual number infected.

However, present knowledge makes it clear that it is inhuman and useless to continue to inflict on sufferers treatment worse than that in vogue during the Middle Ages, namely internment in leprosaria. The fear of such internment aroused in those in the initial stage of the disease, leads them to conceal the infection until it is too late to treat them effectively and there is a risk of contaminating those near to them.

The higher contagiousness of leprosy is a myth. A woman suffering from leprosy can give birth to perfectly healthy children and the risks of contracting leprosy run by those living near a sufferer are infinitely smaller than the risks associated with tuberculosis. Thus the experts felt that it was extremely important to draw attention to the futility and even the danger of the measures for compulsory isolation taken against infected individuals.

Confirming recommendations made in Cairo as early as 1938, the Expert Committee recommended that recourse should be had to segregation only in cases presenting a real danger of infection. If this humane policy is applied, the experts feel that patients will come for treatment voluntarily and will thus themselves help to wipe out the disease.

Furthermore, the Expert Committee noted with satisfaction the progress made in the treatment of leprosy by the use of sulfones. These new synthetic drugs, which were tried out during the second World War, have led to considerable improvement, if not complete cure, being recorded after one or two years' treatment. In addition, they have the advantage that they can be taken by mouth in the form of tablets.

Besides these established and confirmed facts, the experts discussed the hopes raised by observations indicating that BCG may play the same role in the control of leprosy as it does in that of tuberculosis. If this effect of BCG were confirmed, large-scale treatment campaigns could be undertaken in countries where leprosy is endemic.

Of great interest in this connection is the decision of the Director of the Health Services of a South American country (where leprosy is a serious problem) provisionally to drop plans for starting on a large leprosarium and to await the recommendations of the WHO Expert Committee so as to bring his policy for the control of the disease into line with the most modern concepts and methods. The authorities of another country requested, and this was approved by WHO, that the Secretary of the Committee, Dr. R. Chaussinand, assist them after the close of the meeting with his advice in remodelling the leprosy control facilities of the country in accordance with more humane and effective principles.

Leprosy, a contagious disease caused by the development of Hansen's bacillus in the body, and with numerous similarities to tuberculosis, is transmitted by direct and repeated contact and by nasal secretion soiling objects of everyday use (working implements, toilet articles, beds, tables, etc.)

It develops more frequently among the young than among the aged, and among men more than among women. All races are receptive and climate does not play a very important part in its spread, except to the extent that climatic conditions bring about digestive disturbances, malnutrition and a lowering of resistance to infection.

It has frequently been observed that Europeans who have lived in regions where leprosy is prevalent have contracted the disease, and have then recovered *unknown to themselves* after having returned to their native country and to a diet and mode of life better adapted to their constitution.

New Aid for Venereal Disease Nursing

In response to inquiries by public health nursing educators about the nurse's responsibility in the changing pattern of venereal disease control, the Public Health Service, through the Division of Venereal Disease Control in the Bureau of State Services, cooperated with the Georgia State Department of Health in holding a 2-week work conference early in 1951 at the Alto Medical Center, Alto, Ga. Sixteen States and 23 universities were represented by faculty members attending the conference.

An outgrowth of the conference is the publication of a 28-page "Suggested Outline for the Teaching of Venereal Disease Control," by the National League of Nursing Education, 2 Park Avenue, New York 16, N. Y. Divided into three major units, the outline covers: medical aspects of venereal disease; venereal disease within the frame work of nursing; and community education in venereal disease.

The outline is planned to serve as groundwork for revising courses of instruction for the student nurse in venereal disease control. Its use will depend on the individual instructor, the needs and interests of the students, available resources, the scope of the curriculum, and the area where the school of nursing is located. Methods and activities are suggested to the instructor for selecting realistic activities in the development of learning situations.

—*Public Health Reports, U. S. A., Vol. 67, No. 9, Sept. 1952.*

NEWS AT HOME AND ABROAD

Association of Dermatologists & Venerologists, Bombay

The Managing Committee has great pleasure in submitting the fifth Annual report of the Association for the year ending 30th September 1952.

Membership. There were 27 members on the rolls.

Activities. The Managing Committee held 4 meetings during the year to transact routine business. It was decided that the Clinical meetings should be held on the 2nd Wednesday of each month alternately at the K. E. M., G. T.,

Bellasis Road, J. J. and Nair Hospitals. Accordingly 10 meetings, 4 at K. E. M, 2 at J. J., 2 at G. T. one at Nair, and one at Bellasis Road Hospitals were held The attendance was good at each of the meetings. It has not yet been possible to arrange publication of the proceedings of these meetings. Though the clinical meetings were made open to general practitioners by notification in the paper and College and Hospitals' notice boards they did not appear to have taken advantage of these meetings.

Journal. The proposal for the publication of the official Journal of the Association did not materialise and negotiations are still going on with the Bengal Branch so as to arrive at an unanimous decision and it is earnestly hoped to start the Journal at least this year. Plans for the same are ready and the Branch has coopted Drs. Welinkar, Sharat Desai and J. Fernandes as colloborators. On the 17th June the President of the Branch Dr. Welinkar entertained the members to a sumptuous dinner at his residence to give a send off to Dr. P. N. Rangiah of Madras Branch who was proceeding abroad on a W. H. O. Travel Fellowship. All the members were present and the function was a great success.

Tenth International Congress of Dermatology Two of our members Rao Bahadur Dr. H. A. Maniar and Dr. U. B. Narayanarao (Indian Secretary to the Cangress) attended the Cangress which was held at London in the last week of July Other Indian delegates who attended were Drs. Dhurander, Miss. Maniar of Bombay, Drs. D. Panja, and Sanyal of Calcutta, Drs. R. V. Rajam and P. N. Rangiah of Madras.

Annual Meeting. The fourth Annual meeting was held at C. C. I. on 26th February 52. The President of the Indian Medical Association Dr. T. S. Tirumurthi and Secretary of Madras Branch Dr. P. Natesan were the distinguished guests. The new office bearers at the meeting were elected for the year.

The Managing Committee has great pleasure in recording their gratefulness to its President, Dr. Welinker for his cooperation and guidance during the year and conveys its sincere thanks to the authorities and staff of the different Institutions of the city for having made arrangements for our clinical meetings.

Thanks are also due to the honoray auditors Messrs. Hansotia and Co. for auditing our accounts.

British Authority on Leprosy Dead

Dr. Gordon Alexander Ayrie, who has died at his home in Kirkcaldy Scotland, at the age of 52, was a leading authority in the field of leprosy. For nearly 20 years he worked at, and was later in charge of, a model leper colony set up at Sungei Buloh, Malaya. During the Japanese occupation, Dr. Ayrie, at great personal risk, organised the settlement at Sungei Buloh as a base to guide British troops in the jungle and to send food and medical supplies. In January 1944 he was sent to a Japanese labour camp where he remained until liberation.

Recurrent attacks of malaria wrought havoc with his health, and specialists in Britain gave him three years to live. But even in his sickness he went on fighting for lepers.

Wkile in Malaya he paid an occasional visit to centres of leprosy work in India. In 1947 he became medical secretary of the British Empire Leprosy Relief Association (BELRA), a position he held until the end of 1950, when ill-health compelled him to relinquish the post. Before he died Dr. Ayrie learned

with joy that Sungei Buloh, which he and his wife had laboured so bravely to establish, was rising again.

In 1950, shortly before ill-health caused him finally to retire from the struggle which he had waged for so long against leprosy, Dr. Ayrie in an article in a silver jubilee booklet of BELRA wrote of the progress that had been made in the past five years and of the great hopes for the future brought about by the advent of sulphone compounds.

Before, the prospect of anyone suffering from the more severe type of leprosy could be regarded as one of hopelessness and despair. "Today", he wrote, "as a result of sulphone thereapy there is no place for such despair. We have reached a stage where we can definitely say that there is no case of leprosy, however advanced, which can be regarded as hopeless. It is true that the results are sometimes fitful, and that the sulphones are by no means free from danger. However, when all has been conceded, we can definitely say that we have entered upon a new era and provided ourselves with a weapon more potent than anything before known in the history of the disease."

"Nor is that the end. The sulphones have admittedly a number of drawbacks. These have gradually been overcome. Nor has our search for newer and more effective remedies ever halted. Even though today we have robbed leprosy of much of its terror, we can look forward with some confidence to even better, safer and more effective remedies in the future."

—*British Information Services, B F. 447*

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FROM OUR BOOKSHELF

DISEASES OF THE SKIN: A Manual for students and practitioners. First complied by the late Robert W. MacKenna, M. A., M. D., Ch. B. (Edin.); 5th Edition, by Robert M. B. MacKenna, M. A., M. D. (Camb.), F. R. C. P. (Lond.) with a chapter concerning radiology by L. G. Williams, F. R. C. S. (Eng.) D. M. R. E. (Camb.), F. F. R. (Gt. B.); 1952. London: Bailliere, Tindall and Cox. Pp 622, with 215 Illustrations. Price: 42s.

Fifteen years after the fourth edition, the fifth edition of MacKenna's book is completely revised and recast, so as to meet the needs of the Modern Student and practitioner. It gives concise yet adequate descriptions of various skin disorders with sufficient details to enable the differential diagnosis and to institute an effective therapy. The common skin disorders are exhaustively dealt with while rarer one are briefly mentioned. The addition of a large number of prescriptions is an useful feature of the book.

Besides the latest research and advances in radiology and antibiotics pertaining to the dermatological therapy are included. The utility of the book is greatly enhanced by the addition 215 illustrations and 27 coloured plates which are well selected and excellent.

The paper, printing and binding are excellent and the general appearance is very attractive.

It is very useful book for the general practitioner and the student and can also be valuable to the specialist. L. G. B.

SKIN THERAPEUTICS: PRESENTATION AND PREPARATION (MATERIA MEDICA DERMATOLOGICA): By M. K. Polano, with an introduction by Clarence S. Livingood: 1952. Amsterdam: Elsevier Publishing Co., Pp. 290., Price: 37s. 6d.

Besides the internal medication, the topical therapeutics is an indispensable aid in the successful treatment of various dermatological disorders. Some valuable therapeutic agents of one country cannot be followed by another country due to the non-uniformity of nomenclature. Again many proprietary preparation are often prescribed and this makes the external treatment expensive. The efficacy and composition of many of them are not sufficiently known. This practice of prescribing proprietary preparations impairs the skill and efficiency of the pharmacist.

The author has provided in this book a system to facilitate the prescriptions of all medicaments for the dermatological treatment with the help of official pharmacopoeias and formularies. The external treatment with creams, lotions, pastes, ointments etc. are nicely discribed. It also contains valuable instructions to pharmaceutical chemists for the compounding of these preparations.

There is also a table in the end giving a comparative list of dermatological drugs used in American, British, Swiss and Dutch official pharmacopoeias. There is also table giving the Latin and other synonyms of the official American names. In the next ten tables are given the anologous preparations of official Belgian, British, Danish, Dutch, French, German, Italian, Spanish, Swiss and Swedish dermatological drugs.

The author deserve congratulations for having brought together such a mine of information in this valuable book.

The book is very useful to the general practitioners in the treatment of skin disorders and more useful to the dispensary and manufacturing chemist.

The paper printing and binding are excellent and the general get up is attractive.

L. G. B.

INDIGENOUS MEDICINAL SPECIALITIES: By Dr. U. B. Narayanrao, Bombay, Published: By Medical Digest, Girgaum Road, Bombay 4. First Edition, October 1952, Pp. 352, Royal 16th, Price: Rs. 7-8-0, Postage extra-annas eight.

In the Author's preface to the publication, he states "It is essentially a handbook of reference for the busy practitioner who intends to use indigenous remedies. It is hoped that practitioners of all systems of Medicine will find this a day to day reference book". This hope of the Author has every prospect of being amply fulfilled by the excellent manner in which he has managed to put in a vast amount of useful information in the comparatively short compass of about 352 pages of Royal octavo-print a masterly feat, the accomplishment of which is made possible by the indigenous system of abbreviations used by the Author and described by him in section I of the book. The next section (Section II) gives a table of weights and measures of indigenous medicine. Section III gives a List of about 341 drugs alphabetically arranged with their names in different languages, important actions and usefulness of this List may be gathered by a sample of the information given under Abhrak. (The first drug in the list and placed under) "A" which is as follows:—

"Abhrak (Hindi) Abraka, abhra (Sanskrit), Abhra (Bengali), Abhrak (Mahrathi, Gujarati and Canarese). Abhrakam (Telugu), Mica (Latin), Talc or Muscovy glass (English). Astringent, general tonic, aphrodisiac, alterative, acts on the diseases of lungs, removes the derangement of Tridosha and establishes their equipoise." Section IV gives a list of about 21 indigenous medicinal combinations, having special names, like Ashta Warga, Dasha Moola, Chaturjata, Trikatu etc, together with their ingredients, actions and uses. Section V, which is the longest in the book, contains a list of about 838 Indigenous Medicinal Specialities (like Arishta, Choorna, Rasa, Vati, Ghrita, Taila etc) arranged in alphbetical order and giving the name, authority, ingredients, actions and uses of each. These two sections (IV & V) may prove specially useful to the busy general practitioners. Section VI gives an alphabetical list of names of about 113 manufacturers of medicinal preparations containing Indigenous drugs, with their names and addresses. Section VII gives a list, alphabetically arranged of about 694 specialities having indigenous drugs together with the syn. (if any), the chief ingredients, therapeutical uses, contraindications (if any) and dosage of each speciality. Dr. K. S. Mhaskar who writes an appreciative introduction to the publication writes of this list that it "is bound to prove useful to Research workers as it gives them in a handy form much of the required information necessary for investigation work". Section VIII (and the last) gives a Therapeutic index of diseases alphabetically arranged. The reviewer *can well join Dr. K. S. Mhaskar "in recommending this book to the notice of the Medical profession interested in Ancient and Modern Medical Science.*

G. S. M.

OUR SPECIAL OFFERS

The "*Medical Digest*" completes its 20th Volume with the December 1952 issue and the next Volume begins from January 1952. Many improvements will be made in the next Volume i. e. in the get up, reading matter etc.

Any three of the following Symposiums will be posted *Free* on receipt of the annual subscription of Rs. 5/- for *Medical Digest*, by Postal Order (crossed) in the name of "*Medical Digest*", Bombay. 4.

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6. " " June " 3rd "
7. " " July " 4th "

All these symposiums were well reviewed by various Medical Journals and highly spoken by eminent Medical Men etc., in India and abroad.

The Symposium on *Dietetics*-in 4 parts, will also be supplied free to purchasers of Dr. Rao's book entitled : *Indigenous Medicinal Specialities*. 1952, priced at Rs. 7/8/-. & as. 8/- P. Postage.

This *Offer* is available only up to end of June 1953.

All the old and new subscribers of the "*Digest*" are also entitled to become the Subscribers of our quarterly: *Indian Journal of Venereal Diseases and Dermatology*, which is the only one of its kind published in India on the subject-for the year 1953 (January to December '53) at a concessional rate of Rs. 5/8/- instead of Rs. 7/8/- (P. A.) This remittance can be sent along with the form below-duly filled in, on or before the end of *June 1953*.

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